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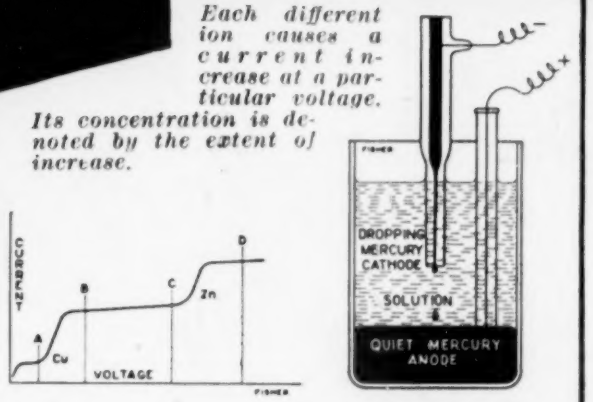

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Recent Theories About the Origin of the Solar System

D. ter Haar

Department of Physics, Purdue University

MANY THEORIES CONCERNING THE ORIGIN of the solar system, starting from a plausible, hypothetical, original situation, have been offered since Descartes, in 1644, made the first attempt to explain the observed regularities of our planetary system.

In the last decade, renewed interest has been shown in this subject, and new theories have been proposed by physicists and astronomers. Before considering these theories in detail, let us summarize briefly those features of the solar system which require explanation. As was long ago pointed out by Laplace, there are so many regularities that the system could not have been formed fortuitously but must be genetically related. This is sufficiently established by the fact that the revolutions of all the planets and asteroids about the sun are in the same direction.

Regularities of the Solar System

The solar system consists of the sun, 9 large planets, 28 satellites revolving about 6 of these planets, more than 1,500 asteroids, and the comets and meteors. Our main concern here will be with the planets.

The regularities shown by the planets may be divided into four main groups:

First, there are the orbital regularities. Apart from the common direction of orbital motion, the eccentricities of the orbits are small, and the orbital planes are practically the same. The rotation of the sun is also in the same direction, and its equator is only slightly inclined to the planetary orbital planes.

Secondly, the mean distances of the planets from the sun obey very closely the so-called Titius-Bode law. This law gives, as the expression for the mean distance of the nth planet from the sun, $r_n = a + b \cdot 2^n$, where $a = 0.4$ A.U. and $b = 0.3$ A.U.[1] and where the group of the asteroids is counted as one of the planets.

The law

$$r_n = r_0 \varepsilon^n \qquad (1)$$

instead of the Titius-Bode law gives us, with about the same amount of accuracy, the mean distances of the planets from the sun.[2] This expression is often more convenient to use, and, when we refer to the Titius-Bode law, we will have in mind expression (1).

For the satellite systems of Jupiter, Saturn, and Uranus laws such as that given in equation (1) apply (with different ε's). Also, the orbits of these satellites show the same regularities as do the planetary orbits.

Altogether, the satellite systems are analogous to the planetary system in so many ways[3] that the conclusion seems unavoidable that the manner of their formation should essentially have been the same.

The third feature of the solar system which requires explanation is that the inner, or terrestrial, planets (Mercury, Venus, the earth, Mars) and the outer, or major, planets (Jupiter, Saturn, Uranus, Neptune[4]) are separated not only in space but also by their physical properties. The inner planets are comparatively small bodies with a high specific density, low rotational velocity, and few satellites. The outer planets, on the other hand, are large, their specific density low, their rotation fast, and their satellite systems extensive.

The fourth and last feature of the solar system which has to be explained is the distribution of the

[1] One A.U. (astronomical unit) = mean distance of the earth from the sun = $1.5 \cdot 10^{13}$ cm.

[2] For the planetary system, $\varepsilon = 1.67$. Incidentally, the accuracy of the results obtained in some astrophysical problems is far less than that with which physicists are often used to working. The Titius-Bode law is, for instance, more a rule of thumb for finding the distances of the different planets than a law which is obeyed within a few per cent. The same impossibility of obtaining very accurate results can, for example, be seen when we consider the table on page 410 to give an excellent agreement between the observed and calculated masses. But, even so, it seems that the exponential laws for the distances of the planets and satellites from the sun and primaries are more than just a coincidence (cf. 6).

[3] Apart from the fact that there exist exponential laws for the mean distances of the satellites from their primaries, and that their orbits show regularities, the distribution of the angular momentum in the systems formed by the satellites with their primaries is very similar to that distribution in the planetary system. The sun's angular velocity is smaller than the angular velocity corresponding to Kepler's third law by a factor of 200. This factor is not quite so large in the case of the outer planets but ranges there between 3 and 6, which is still considerable. Finally, the ratio between the masses of the central body and the revolving satellites is about 1 : 1,000 both in the cases of the outer planets and in the case of the sun.

[4] We shall not discuss Pluto in this paper. This planet is small and dense, and its orbit has a large eccentricity. It thus differs considerably from the other outer planets.

angular momentum. The sun possesses about 99% of the mass of the total solar system, but only 2% of the total angular momentum. Failure to explain this point has caused the downfall of many theories in the past, the most notable being those of Kant and Laplace.

We may indicate here, briefly, the difficulties, first pointed out in 1884 by Fouché, inherent to the distribution of the angular momentum. The angular velocities of the planets are determined by their mean distances from the sun in accordance with Kepler's laws. The strange thing is not that the planets have such a large angular momentum but that the sun rotates so slowly.

If one attempts to account for the origin of the solar system by some kind of catastrophe, this accident may have brought about the present distribution of the angular momentum. If, however, one tries to develop a theory starting from the sun alone, perhaps surrounded by a gas cloud, it is not easy to see how the average angular momentum per unit mass should be so much lower for the solar than for the planetary matter.

Of course, the four main groups of regular features mentioned above are not the only ones exhibited by the solar system. We will not discuss here the other properties of the solar system, such as the Saturnian rings or the asteroid system. Some of these irregularities can be explained easily, while others still await an acceptable explanation.

Prior to a discussion of some of the new theories proposed during the last 10 years, it should be pointed out that all theories about the origin of the solar system can be divided into two groups, according to whether or not they assume an interaction with other celestial bodies as an integral part of the development of the solar system. In the first case, we have an open system; these theories are called *dualistic* or *catastrophic*. In the second case, the system is closed, and the theories are called *monistic* or *uniformitarian*.

For a critical survey of older theories, the reader is referred to the many excellent textbooks written on the subject (*10*). Here the discussion will be confined to the recent dualistic theories of Lyttleton and Hoyle and the recent monistic theories of Alfvén, Whipple, Berlage, von Weizsäcker, and ter Haar. A detailed criticism of these theories will be given in a forthcoming paper (*6*).

Binary Theories

Russell (*10*) pointed out that the tidal theories of Jeans and Jeffreys are unable to explain the distribution of the angular momentum, although, at first sight, the encounter of a second star with the sun seems to be able to provide the system with sufficient angular momentum. Russell himself suggested as a possible, though not very promising, way out that the sun might have been a binary star whose second component was removed by some kind of a catastrophe.

Lyttleton has followed up this idea and given two different theories along those lines. The first one (*8*) followed Russell's idea very closely and assumed that a third star collided with the sun's companion. In that way, the binary system may have been broken up and a gaseous filament provided which would thereafter condense into the planets in a way analogous to the condensation in the tidal theories. Although it seems that Luyten's criticism is not valid, there are still too many difficulties connected with this theory for it to be accepted as a final solution, *e.g.* we may mention here Lyttleton's own difficulty in accounting for the satellite systems.

The alternative solution suggested by Lyttleton (*9*) also meets with the same difficulties. In this theory he starts from a triple star. The two companions of the sun are supposed to form a very close binary. During the evolution of this binary system, they will draw closer to each other and finally the two stars will combine into one mass. This mass will, however, be rotationally unstable and will consequently break up. The result of the fission of the combined mass will be that the two fission products will leave the system, leaving behind them a gaseous filament. The further development follows the same line as in Lyttleton's original theory.

According to another Cambridge astronomer, Hoyle (*7*), who has indicated a third possibility, starting from a binary system, a supernova outburst of the sun's companion may have resulted in the breaking up of the binary system and the production of a gaseous filament. From data concerning the Chinese supernova of 1054 A.D., which was presumably the origin of the Crab nebula, Hoyle concludes that this process might not be completely impossible. His theory, however, seems to encounter even more obstacles than Lyttleton's theories.[5]

Alfvén's Theory

The Swedish physicist, Alfvén, has proposed a most interesting theory which takes into account the magnetic moment of the sun (*1*). This was previously done by the Norwegian scientist Birkeland, but he never followed up this idea by proposing a really detailed cosmogony.

Alfvén had two reasons for advancing this theory: (1) The magnetic force on charged matter due to the

[5] Spitzer (*11*) has shown, for instance, that such a hot filament will disappear by evaporation before it can cool down sufficiently to allow condensation to take place.

sun's magnetic field exceeds by far the gravitational force of the sun on the same matter in the regions of the solar system. (2) He had shown in an earlier paper that the rotating magnetic moment of the sun is able to cause currents in a neighboring ion cloud. Because of these currents the ion cloud will start to take part in the solar rotation, and the sun will be decelerated. In this way, an appreciable amount of angular moment can be transferred from the sun to such an ion cloud in a period of 10^5 years. This is short compared with the age of the solar system, which is of the order of magnitude of 3,000,000,000 ($3 \cdot 10^9$) years. The present distribution of the angular momentum is in this way easily explained.

Alfvén now proposes the following process for the formation of the outer planets: The sun is supposed to be surrounded, at a certain stage of its life, by an interstellar gas cloud. Due to the gravitational attraction of the sun, the atoms in the cloud will start falling toward the sun, and their kinetic energy will increase because of the gain of gravitational energy. Eventually, this energy will become so large that ionization through collisions will take place. Once an atom is ionized, the movement is arrested, and the ion has to move along the magnetic lines of force to an equilibrium position in the equatorial plane of the sun. In this way, Alfvén obtains a mass concentration in the equatorial plane. In this gaseous disc, condensation will take place, resulting in the formation of the planets.

This mechanism, though giving a possible solution for the formation of the outer planets, cannot account for the inner planets. The distance from the sun at which ionization occurs is too large to get any mass in the regions where the inner planets are observed. Alfvén suggests, therefore, without any detail, a different process for the formation of the terrestrial planets. He assumes that, at another stage of the sun's journey through space, it may have met an interstellar smoke cloud consisting of small solid particles. These particles will sublimate in the vicinity of the sun, the resulting atoms will become ionized, and a process similar to that described above will start, but at less distance from the sun.

A quantitative analysis of the processes discussed by Alfvén shows that they could never have played an important part in the formation of our solar system. In a gaseous system surrounding the sun which contains sufficient mass to provide for the planets, ionization will be completely negligible (*6*). However, if the sun collected the matter of the planets during its journey through space, it can be shown that it is impossible to collect sufficient material in the way described by Alfvén.

The Dust Cloud Hypothesis

Recently, Whipple (*13*) has introduced an entirely new idea into this old problem. As yet, this idea has not developed into a theory, and it seems questionable whether this is possible.

Whipple starts from a cloud in which gas and smoke particles[6] are mixed. The contraction of this cloud, which has an original radius of about 30,000 A.U., should produce both the sun and the planets.

To account for the low angular momentum of the sun, the cloud is assumed to possess negligible angular momentum. The planets are assumed to be formed in a stream in the cloud. It is assumed that in this stream there are concentrations of matter which will ultimately produce the planets. Because the planets are formed in the stream, they will possess from the beginning the necessary angular momentum. On their path through the large cloud, these proto-planets will sweep up matter with zero angular momentum and consequently spiral inward.

The solution for the present distribution of the angular momentum is included in the theory from the beginning, so that this point presents no difficulties. The small eccentricities of the orbits are produced by the accretion process, as in the tidal theories of Jeans and Jeffreys. Whipple has not as yet studied the further development of these proto-planets closely enough to be able to explain any other properties of the system, and it seems extremely doubtful whether this will be possible.

A Revival of Kant's Theory?

As is well known, the theory proposed in 1755 by Immanual Kant in his "Allgemeine Naturgeschichte und Theorie des Himmels," and given in a mathematical form by du Ligondès in 1897, was regarded as disproved because of the impossibility of understanding the present distribution of the angular momentum.

At present, however, it seems that this *communis opinio* was due to a misunderstanding of the problem, and quantitative calculations appear to show, to the contrary, that Kant's theory is probably the most promising of all existing theories.

The first author to start again from the same initial system as the one studied by Kant was the Dutch meteorologist, Berlage (*2*). He tried to combine Kant's and Laplace's theories by investigating the possibility of the formation of a system of rings in a gaseous disc surrounding the sun. From these rings

[6] This is a better name than dust particles for the solid particles existing in interstellar space, as was first remarked by van de Hulst (*5*) following the nomenclature of physical chemistry, where smoke is the product of a condensation process.

the planets should have been formed by condensation in these rings, in Laplace's theory.

The second attempt was made by the German nuclear physicist, von Weizsäcker (*12*). His theory, which was dedicated to Sommerfeld on the occasion of his 75th birthday, will be discussed here in some detail, since von Weizsäcker draws attention to a few new features of the problem. Although his attempt seems also doomed to fail, his manner of attacking the problem can help us to explain many of the features of the planetary system.

First of all, von Weizsäcker shows that a gaseous envelope around the sun which possesses an angular momentum will assume a disc shape because of its rotation. The disc, however, is not stable. It can be shown that the velocities in the disc will follow Kepler's third law rather closely, *i.e.* the angular velocities decrease as the square root of the distance from the sun. Due to the differences of velocities, viscous forces will be present, striving to set up a rotation of a rigid body. The outer parts of the disc will thus be accelerated and move outward on account of the increased velocity, and the inner parts will be decelerated and move toward the sun in the center. Eventually, the disc will dissolve completely.

This dissipation of the disc is thus accompanied by three phenomena. First of all, the viscous stresses spend energy; this energy is provided by the matter falling onto the sun and gaining gravitational energy. Secondly, there is a transfer of angular momentum from the inner to the outer parts of the system. Thirdly, the matter of the system is dissipated, part of it falling on the sun, and the other part evaporating into space. Von Weizsäcker uses this dissipation to explain the present distribution of the angular momentum. He assumes that the matter falling on the sun possesses zero angular momentum, and that the matter flying away into space has a low atomic weight and possesses the bulk of the angular momentum. In this way, he obtains a slowly rotating sun and is at the same time able to explain that the planets contain more heavy elements than the sun.

There are two objections to this solution. The first is that it seems improbable that there should occur such a separation according to atomic weight and angular momentum. Secondly, it turns out that the total deceleration of the sun due to this accretion of matter with zero angular momentum is too small to account for the slow rotation of the sun, by a factor of the order of magnitude of at least 100,000.

The next step in von Weizsäcker's theory is the consideration of a pattern of vortices which might have existed in the disc. He shows that if we may assume that the orbits of the mass elements in the disc are unperturbed Keplerian ellipses, a regular system of vortices, like that shown in Fig. 1, can be built up. If the rotation of the disc is direct (counterclockwise), the movement in the vortices will be clockwise.

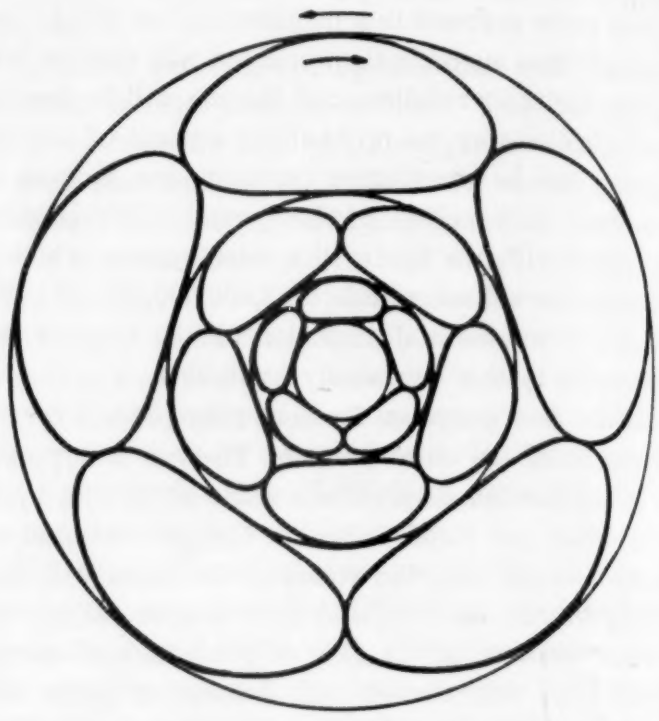

FIG. 1. The outer arrow indicates the direction of rotation of the whole disc, while the inner arrow indicates the direction of rotation in the vortices. The sun is in the center of the whole system.

Von Weizsäcker considers this system for two reasons. First, gravitational forces are by far the most important forces in the disc, so that the orbits in the disc would be Keplerian if there were no collisions. Secondly, the energy dissipation will be less in a regular system such as that shown in Fig. 1. The dissipation will take place along the circles where the rings of vortices meet. The viscous stresses along those circles, separating the main vortices, will give rise to secondary eddies. As can be shown, conditions for condensation will be more favorable in these "roller bearings," which means that we may expect the planets at distances from the sun, corresponding to the radii of these circles. In a system like that pictured in Fig. 1, the ratio of the radii of two consecutive circles is constant, thus presenting us with the exponential Titius-Bode law (*10*).

However, von Weizsäcker's reasoning cannot be accepted as final, since the mean free path in the disc is only a few inches because of the density in the disc necessary to provide sufficient matter for the planets. The unperturbed Keplerian orbits necessary to derive the regular system of vortices of Fig. 1 seem to be out of the question. Instead, one has to apply hydrodynamics. Although there are indications (*6*) that, indeed, a regular system of vortices might be a solution of the hydrodynamical equations, the above explanation of the Titius-Bode law and similar laws

for the satellite systems has as yet to be accepted with reservation. It is to be hoped that a study of the quadratic hydrodynamical equations may give a final answer as to whether a regular system of vortices has once existed in the gaseous disc.

During the formations of the planets they would be surrounded by an extended atmosphere. It is reasonable to assume that the formation of the satellite systems in these atmospheres would be analogous to the formation of the planets in the original gaseous disc.

Von Weizsäcker finally gives a qualitative picture of the condensation process, showing that the period necessary to build up bodies of the size of the planets is of the same order as the estimated lifetime of the disc.

Latest Developments

In view of the fact that none of the existing theories seemed to give a satisfactory solution, ter Haar (*6*) tried to investigate in detail the properties of a gaseous, rotating solar envelope. A second reason for adding a new theory to the many which already exist was that no one had up to that moment given a *quantitative* analysis of the condensation process.

A short survey of this investigation will be given here, and it will be shown that by means of Kant's theory the differences between the inner and the outer planets may be explained.

As remarked above in the discussion of von Weizsäcker's theory, the explanation of the Titius-Bode law is still an open question. That point will not be discussed further here.

The first step in a quantitative analysis of Kant's theory ought to be a discussion of the physical and hydrodynamical aspects of the solar gaseous envelope, which will contain originally about one-half of the solar mass, and the density of which will be about 10^{-9} g cm^{-3}.

This analysis shows that the envelope will have a disc shape, *i.e.* the density decreases outward and in directions perpendicular to the equatorial plane of the sun. It also shows that ionization is negligible, and that the temperature in the disc will decrease as the inverse square root of the distance from the sun. At a distance corresponding to Mercury's mean distance from the sun the temperature will be about 650° K, decreasing to about 75° K in the vicinity of Neptune. For the mean distance of the earth from the sun, we have about 400° K.[7]

The hydrodynamical analysis enables us to calculate the rate of energy dissipation and, hence, the lifetime of the disc. Part of the matter in the disc falls on the sun, thus gaining gravitational energy; this process provides the energy lost in the dissipation process. The lifetime of the disc turns out to lie between 10^7 and 10^8 years. As we remarked before, the energy dissipation is a consequence of the viscous stresses in the disc, due to a velocity gradient corresponding to Kepler's third law. These viscous forces entail also a transfer of angular momentum. The inner parts of the disc will be slowed down. This process is analogous to the drag of a viscous fluid on a rotating disc, used to determine the viscosity coefficient.

It is possible to make a rough estimate of the transfer of angular momentum in the disc per unit time. Since it is also possible to estimate the lifetime of the disc, we are able to estimate in first approximation the total deceleration of the sun during the formation of the planetary system. Although the results are still far from final, it seems that the low rotational velocity of the sun cannot possibly be explained in that way.

Following analysis of the physical and hydrodynamical properties of the gaseous disc, the condensation process has to be considered quantitatively.[8] The condensation process can be divided into three phases: (1) the formation of nuclei for further condensation, (2) the growth of these nuclei, and (3) gravitational capture. The growth during the last stage is much faster than that during the first two stages.

Stages 1 and 2 are analogous to the formation of drops in a supersaturated vapor. From the theory of condensation it follows that the temperature determines which compounds are supersaturated at a given density. Whether or not a certain compound is supersaturated at a given temperature and density depends on its heat of sublimation. If the heat of sublimation is larger than a critical value, the compound will be supersaturated, otherwise not. The critical heat of sublimation is mainly determined by the temperature and depends only slightly on the density.

In the gaseous disc, the temperature decreases with increasing distance from the center. Consequently, in the regions nearer to the sun fewer compounds will take part in the initial condensation phases than in the outer regions of the solar system. It now turns out that, in the regions of the solar system where the terrestrial planets are found, only inorganic compounds will condense. In the regions

[7] The fact that the observed surface temperatures of the planets are lower by a factor 1.4 is due to the planetary rotation. The sun heats up only the part of the planet facing the sun. This factor was overlooked by von Weizsäcker.

[8] We may remark here that in the planetesimal theory of Chamberlin and Moulton (*4*) similar considerations were given, though those authors did not discuss the processes very extensively and quantitatively.

of the outer planets, however, both organic and inorganic compounds can condense. It is very remarkable that the change-over from inorganic to organic compounds lies just in the region between the inner and outer planets.

This has two consequences. First of all, there will be fewer condensation nuclei in the inner parts of the system than in the outer parts. Secondly, the specific density of the condensation nuclei in the inner regions will be higher than that of the nuclei in the outer regions. From this alone, we could already expect heavier, small inner planets and light, large outer planets.

This precipitation of the supersaturated compounds will continue until the bodies have become so large that gravitational effects will become important. The gas molecules are then captured in the gravitational fields of the condensation products, and the protoplanets will grow very fast until the gas is exhausted.

The bodies for which gravitational capture begins to play a role are of about the same size as Venus. From this, we see that this last stage has not been important in the building-up process of the inner planets. For the outer planets, however, gravitational capture has been important, thus increasing their mass and decreasing their specific density because of the capture of the light compounds which were not supersaturated even at temperatures of about 100° K.

The reason why the outer planets have grown beyond the second stage, and the inner planets not, is that the lifetime of the disc is of the same order of magnitude as the time necessary to reach the stage of gravitational capture. The inner planets grow more slowly than the outer planets during the first two stages because fewer compounds play a part in these stages. Therefore, the outer planets may well have reached the third stage before the dissipation of the disc became important, but when the inner planets had attained that size, the dissipation of the disc prevented an appreciable further growth.

It is possible to explain even the small differences in density of the various planets. Brown (*3*) has shown that, if one assumes that all the inner planets are built up from the same material, their densities will vary because of a variation of pressure in their interior, due to their varying masses. As for the outer planets, we have to assume that they are built up of heavier material plus some lighter gases captured during the last stage of their formation. In that way the differences in density can all be understood.

We will assume now that in the building up of the outer planets about 20 times as much of the matter in the disc has taken part as in the formation of the inner planets, corresponding to the fact that for the outer planets gravitational capture has been important. We can then estimate the masses of the planets if they should have been formed in the disc at their present distances from the sun.

In Table 1 we have inserted the values of the planetary masses, calculated under this assumption. The masses are expressed in the earth's mass as unit.

TABLE 1

Planet	Observed mass	Calculated mass
Mercury	0.05	0.1
Venus	0.8	0.5
Earth	1	1
Mars	0.1	2
Jupiter	318	130
Saturn	95	90
Uranus	15	20
Neptune	17	3
Pluto	0.9	0.8

The agreement between the calculated and the observed masses seems to be quite good.[9]

In order to get sufficient mass to build up bodies of the size of the present planets, it appears that the original solar envelope must have contained between one- and five-tenths of the solar mass, because only part of the matter can take part in the condensation process.

During their formation, the outer planets would be surrounded by extended atmospheres. The evolution of these atmospheres will probably be analogous to the evolution of the solar envelope. In this way we have a mechanism for the formation of the satellite systems. Since these atmospheres will be large for the outer planets, and practically absent for the inner planets, we can readily understand why the outer planets are surrounded by extensive satellite systems while the inner planets possess only a few satellites.

For a discussion of the extent to which the various properties of the satellite systems can be explained the reader is referred to ter Haar's paper (*6*). The analysis of these planetary atmospheres gives us also an explanation of the fact that the outer planets rotate faster than the inner ones.

In conclusion, it seems that Kant's theory is stronger than was suspected for a long time. This is rather satisfying, since Kant's theory starts from probably the simplest possible hypothesis—a sun, surrounded by a gaseous envelope.

References

1. ALFVÉN, H. *Stockholms Observ. Ann.*, 1942, **14**, No. 2.

[9] The only serious discrepancy is Mars' mass. It may well be possible that the small mass of Mars is due to the same, as yet unknown, process which prevented the formation of a planet between Mars and Jupiter.

2. BERLAGE, H. P., JR. *Proc roy. Acad. Sci., Amsterdam,* 1940, **43**, 532, 557.
3. BROWN, H. S. *Astrophys. J.*, in press.
4. CHAMBERLIN, T. C. *The origin of the earth.* Chicago: 1916; MOULTON, F. R. *An introduction to astronomy.* New York: 1906. P. 463.
5. TER HAAR, D., VAN DE HULST, H. C., OORT, J. H., and VAN WOERKOM, A. C. C. *Ned. Tijdschr. Natuurkunde,* 1943, **10**, 238.
6. TER HAAR, D. *Proc. roy. Danish Acad.*, in press.
7. HOYLE, F. *Proc. Camb. phil. Soc.*, 1944, **40**, 256; *Mthly Not. R.A.S.*, 1945, **105**, 175.
8. LYTTLETON, R. A. *Mthly Not. R.A.S.*, 1938, **98**, 536.
9. LYTTLETON, R. A. *Mthly Not. R.A.S.*, 1941, **101**, 216.
10. POINCARÉ, H. *Leçons sur les hypothèses cosmogoniques.* Paris: 1913; NÖLKE, F. *Das problem der Entwicklung unseres Planetensystems.* Berlin: 1919; RUSSELL, H. N. *The solar system and its origin.* New York: 1935; RUSSELL, H. N., DUGAN, R. S., and STEWART, J. Q. *Astronomy I.* (Rev. ed.) New York: 1945.
11. SPITZER, L., JR. *Astrophys. J.*, 1939, **90**, 675.
12. VON WEIZSÄCKER, C. F. *Z. Astrophys.*, 1944, **22**, 319; CHANDRASEKHAR, S. *Rev. mod. Phys.*, 1946, **18**, 94.
13. WHIPPLE, F. L. Paper presented at Chicago Meeting of AAAS, December 27, 1947.

The Neurological and Behavioristic Psychological Basis of the Ordering of Society by Means of Ideas

F. S. C. Northrop

Sterling Professor of Philosophy and Law, Yale University

WHAT, SPECIFICALLY, DOES IT MEAN to assert that human behavior and its attendant social institutions are significantly determined as to their form by ideas? For one thing, it means that human beings in society are reacting not merely to particular natural events occurring just once at a given time and place, but also to symbols, to socially conditioned symbols, which keep their meanings constant during the period of decades or centuries, as the case may be, in which a given normative social theory captures their faith and thereby serves as a norm for their social behavior and cultural institutions. But to say that human beings in society are reacting to natural events is to say that their behavior is determined by what is called a particular. And to say that human beings are reacting to symbols which keep their meanings constant through many events is to say that they are reacting to particulars which are the embodiments of universals.

This permits the basic problem of the present inquiry as a whole to be put more specifically. This problem has to do with the relation between ideological and biological factors in social institutions. It has been noted that social institutions embody normative social theories and that these normative social theories are a significant cultural factor in the ordering of social phenomena. But we have just noted, also, that normative social theories, unlike specific events in nature, exemplify universals rather than mere particulars. Thus, our problem of determining the relation between cultural factors and biological factors in social science becomes, in part at least, that of determining the relation between the processes of biological systems and the responses of people to particulars which embody universals.

But there is a second, more specific, portion of our over-all problem. When a given people are captured in the realm of their normative beliefs by a specific normative social theory, this theory serves in their behavior as an end. In other words, it defines a purpose. This means that if we are to clarify the relation between cultural factors and biological factors in social phenomena, we must determine the relation of normatively defined purposes to biological systems.

Previous attempts to solve this problem have produced two conflicting conclusions, which, nevertheless, rest upon a common assumption.

One conclusion was that, since human behavior exhibits responses controlled by purposes defined in terms of remembered norms which are universals rather than merely responses determined by physical events which are particulars, human behavior must therefore have its basis in extra-empirically verifiable extra-biological factors. The assumption here is that in the realm of the biological there are only mechanical causes and no purposes, only particular events and no remembered events with their persistent meanings and hence no universals. This has been the answer of the Cartesian and Lockean dualists on the one hand and of the idealistic philosophers and the German social scientists, with their distinction between the

Address of the vice-president and chairman of the Section on History and Philosophy of Science (L), AAAS, delivered at the joint Symposium (with Section K) on the Relation Between Biological and Cultural Factors in Social Problems, December 28, 1947, in Chicago, Illinois. This address is the middle section of a much longer article entitled "Ideological Man in His Relation to Scientifically Known Natural Man," in the symposium volume, *Ideological differences and world order*, which is to be published in 1948 for the Viking Fund by the Yale University Press.

Naturwissenschaften and the *Geisteswissenschaften* on the other. Purpose, memory, and the existence of universals, they maintain, unequivocally establish the existence and reality of nonbiological minds or mental substances or of a priori autonomous moral principles in human nature and social phenomena.

The other conclusion, represented by the early mechanistic biologists, the behavioristic psychologists, and the positivistic British and French social scientists and philosophers, was that, since biological systems and all natural systems, as known by the methods of natural and biological science, are mechanical systems responding to stimuli which are particulars rather than universals, purpose is a mere appearance or epiphenomenon, and all ideas are particulars. Hence, universals do not exist, being, like the normative theories defined in terms of them, mere semantically misunderstood symbols which, when correctly analyzed, turn out to be either mere pseudorationalizations after the nonpurposefully-caused particular social facts or expressions of purely hortatory and noncognitive significance.

No two schools of thought would seem to be more unqualifiedly opposed than these. Nevertheless, the important thing to note about these two traditional conflicting answers to our problem is the basic premise upon which they agree. This premise is that scientifically verified knowledge of biological and other natural systems provides no meaning for purposes, universals, or human behavior which is a response to, and specified as to its form by, a temporally persistent, normative social theory.

What is the present scientific status of this basic premise?

Recent investigations by Warren S. McCulloch and Walter Pitts show not merely that certain biological organisms, because of the character of the neuron nets in their nervous systems, must know universals, responding to symbols as their exemplars rather than as mere particulars. Other investigations by Arturo Rosenblueth, Norbert Wiener, and Julian Bigelow show that not merely a human being but also robots with inverse or negative feedback mechanisms have purposes that define their behavior. When this purpose can be determined by information, such robots are called servomechanisms. In other words, the basic premise of both the traditional philosophical dualists and idealists and the traditional, supposedly scientific naturalists and mechanists, to the effect that natural and biological systems can have neither knowledge of universals nor normatively defined and behavior-controlling purposes, must be rejected.

The scientific demonstration of these exceedingly important conclusions of revolutionary significance for natural science, moral as well as natural philosophy, and for one's theory of the normative factor in law, politics, religion, and the social sciences, must now concern us.

The traditional theories rest upon an oversimplified notion of activity in the nervous system. They assume that neurons are always put together in the nervous system to form a path in or through the nervous system which is noncircular.

Consider the simplest possible case of a noncircular ordering of the nerve cells called neurons—namely, the case of one afferent neuron, *a*, joined by a synapse to one efferent or motor neuron, *b*. Assume, also, that the signal which is the firing of neuron *a* entails the behavioristic response which is the firing of neuron *b*. Then, assuming no further action upon *a*, the signal which is the firing of *a* perishes as soon as *a* has fire. Hence, the response of neuron *b* is a response to a signal which is a mere particular. The number of noncircularly ordered neurons does not alter this conclusion. It follows, therefore, that if there were no circular paths within or through the nervous system, a signal (*i.e.* the firing of a neuron) at any point within it could signify only what happened at a particular instant; there could then be neither purpose nor memory, and every action would be a response to a mere particular.

Suppose, however, for example, that there are 5 neurons, *a, b, c, d,* and *e,* ordered in a circle in such a way that the signal which is the firing of *a* fires *b,* which signal in turn fires *c,* which, by way of the firing of *d* and *e,* in turn fires *a*. Then, assuming that the time it takes the impulses to succeed one another around the circuit is sufficient to permit any neuron to restore its energy from the metabolic processes of the body, the signal which is the firing of *a* or of any one of the 5 neurons in the circular net will not perish. It will thereby persist through time. In other words it will signify a universal rather than a mere particular. Also, memory will be achieved.

More than a century ago Majendie and Bell had defined reflexive activity and indicated its circular path from a part of the body, through the nervous system, and back to the same part of the body. Cannon and his collaborator, Rosenblueth, were the first to call attention to this homeostatic property and to attempt to extend the concept to relations between the body and the world about it. But it was R. Lorente de Nó (*3*) who postulated and demonstrated the action of what he called reverberating chains of neurons, so arranged in closed paths that each excited the next one around the loop, the last finally exciting the first. Thereby the activity continued to regenerate itself around the loop.

Suppose, also, that an afferent neuron from a sense organ such as the eye excites one of the neurons in

the regenerative loop. And in order not to mix in the same sentence words from different worlds of discourse, let us assume, in addition, that the epistemic correlate (*4*) of the postulated momentary signal or impulse which is the firing of this efferent neuron is in the consciousness of the person in question, the sense datum or "idea" denoted by the word "blue." Assume, also, that an impulse from the eyes fires a neuron which is a member of a regenerative loop and that its impulse is the epistemic correlate of the introspected "idea" or datum, "blue." It follows from the character of a regenerative loop that this impulse will be transmitted continuously without ceasing around the loop, so long as the energy necessary to restore the neurons to a capacity to fire is maintained by metabolic activity. As McCulloch has put the matter, "a train of impulses in a regenerative loop preserves the form of the fact without reference to the one particular moment when it was experienced." In other words, one has the form of the fact remaining constant over time through different particular events. Hence, as McCulloch and Pitts have noted, one has (the epistemic correlate of introspected) universals.

In their first paper on the subject, entitled "A Logical Calculus of the Ideas Imminent in Nervous Activity," McCulloch and Pitts (*2*) have demonstrated, also, that very simply related neural nets made up of such regenerative loops have all the formal properties of the primitive ideas and postulates of the theory of the foundations of mathematics and deductive reasoning of Russell and Whitehead's *Principia Mathematica*. In other words, human nervous systems can reason deductively, and, in so far as they possess and use nervous nets with this formal character, they must reason deductively in precisely the manner specified by an analysis of deductive reasoning and calculation in modern mathematics and symbolic logic. No manifestation of the use of universals and of rationalistic reasoning with universals could be more pure or unequivocal than that occurring in the deductively formulated theories of mathematical physics and mathematics. This means that deductively formulated theories, whether they be the normative theories of social science or the factual, deductively formulated theories of natural science of a Newton, Willard Gibbs, or an Einstein, are not epiphenomena of no causal significance; they are not mere rationalizations after the facts. Instead, because of the formal properties of the neural nets with their impulses in the central nervous systems of human beings, they are scientifically verifiable factors and scientifically verifiable factors of causal significance.

McCulloch and Pitts, in their 1943 paper, proved one other exceedingly important theorem. This theorem is that any robot or organism constructed with regenerative loops possessing the aforementioned formal properties, and thereby being a Thuring machine, "can compute any computable number or, what is the same thing mathematically, can deduce any legitimate conclusion from a finite set of premises." It is not an accident that John Von Neumann and Norbert Wiener, in their designing of two of the most powerful contemporary machines for carrying through mathematical deductions and calculations, and McCulloch and Pitts, in their theoretical and experimental studies of the human nervous system, have influenced one another.

A neuron in a regenerative loop of neurons may be so related to a motor neuron that it not merely fires the neurons in the circle of its own loop, but also fires a motor neuron, thereby producing a specific overt response of the system. When this happens, the constant universal becomes manifest in a particular again, as a specific event here and now, but conforming to its universal.

Furthermore, with many regenerative loops in a single nervous system there can be many universals, and by joining these loops universals can be related. Thereby the postulates of any deductively formulated theory in natural science or any normative theory in social science can be constructed. As long as this related system of impulses in reverberating circuits never fires a motor neuron, it remains a covert universal, a mode of possible action, rather than a particular, or an overt, act. But when it fires a neuron leading out of the circuit, it generates a particular objective event. Thus, we are able to understand how an abstract normative social theory—itself a mere universal and a possible—can, if it gets into a nervous system so as to define the form of its activity, determine the pattern of firing of motor neurons, and so, literally, causally, and neurologically determine an overt, objective, social and institutional fact.

Furthermore, if such a deductively formulated set of postulates is a theory in natural science, it can generate behavioristic responses upon the part of a physicist which put the theory to an empirical test with respect to particular events or facts in nature. Thereby the universals of the deductively formulated theory considered as a possible become related to particulars in a manner which introduces the quantifiers "all" and "some" of Russell and Whitehead's logic of propositional functions into the formal properties of neurological human behavior. This occurs when, as McCulloch has put it, "the universals are referred to the semels (the onces)."

There is, however, nothing to prevent man from constructing several different deductively formulated theories in natural science or in normative social science out of the universals which regenerative loops

provide for him. It may, and does, happen that the firing of a motor neuron prescribed by one normative social theory is proscribed by another. Witness the capitalistic and the communistic theories known to all representatives at the recent Conference of Foreign Ministers. Two such theories in one brain make choice obligatory for action. McCulloch, in his James Arthur Lecture (*1*) delivered on May 2, 1946, put the matter as follows:

> How can the structure of the nervous system embody the possibility of choice? Clearly, if each circuit had a path separate from any other path each would go its own way to its own end. But many paths share nervous parts and others would result in contrary acts of some effectors. A few, like swallowing and drawing breath, working at once would destroy us. Conflicts and mental collisions are barred by inhibitory links from one circuit to another so that when both are excited only one works. Thus the net embodies the possibility of these decisions.

In their 1947 paper, McCulloch and Pitts have carried their neurological theory of our knowledge of universals even further. Newton, among others, pointed out that the structure of sensed space and time is relative to the particular observer and quite different from the structure of public, mathematical space and time to which the theories of experimentally verified physics refer. Einstein continues this Newtonian distinction. An adequate, neurologically grounded theory of knowledge must account, therefore, for the manner in which the knower distinguishes the public, indirectly verified, postulationally designated structures and entities of natural science from the immediately sensed ones. This entails an account of how the nervous system, which receives impulses epistemically correlated with images varying from moment to moment and standpoint to standpoint, arrives at invariant entities and relations holding constant through the changing, immediately apprehended particulars. McCulloch and Pitts have shown that such invariants can be achieved by complicated neural nets which scan and average over a group of transformations. In their 1947 paper not merely do they draw complicated neural nets which have this capacity, but they also give empirical neurological evidence that certain neural nets of actual nervous systems are of this character. Clearly, human nervous systems have the formal properties necessary to know universals and to construct deductive theories in natural science and in factual and normative social science which can causally determine particular human behavior and, through that human behavior, the character of cultural institutions.

It remains to see how neurological systems can be purposeful systems.

In any scientific inquiry the question being asked is crucial. With respect to the study of any behaving system, be it man, beast, or machine, Rosenblueth, Wiener, and Bigelow (*6*) note that there are two different but complementary types of scientific inquiry which one may pursue. The first type they term behavioristic; the second type, functional.

In a behavioristic inquiry one ignores the inner constituents of the system and their relations within it. One concentrates attention, instead, upon what happens with respect to the response of the system when, everything else being kept constant, some specific stimulus or input is brought to bear upon it.

In a functional study, on the other hand, the central subject matter under investigation is the intrinsic structure and internal properties of the system itself. In such a study the input and output are used merely to throw light on the character of the system which connects the one to the other.

In the investigations of both McCulloch and Pitts and Rosenblueth, Wiener, and Bigelow the subject under investigation is a behaving, biological system. The former's approach is functional; the latter's, behavioristic. Yet each throws light upon the other.

Behavior is defined by Rosenblueth, Wiener, and Bigelow as "any change of an entity with respect to its surroundings." The usefulness of such a broad definition appears only when behavior is classified.

Their first dichotomy is between that which is active and that which is passive. In passive behavior, "the object is not a source of energy; all the energy in the output can be traced to the immediate input. . . ." Active behavior, on the other hand, is that "in which the object is the source of the output energy involved in a given specific reaction." The response of a motor neuron not recently fired and fully stored with energy from continuous metabolic processes in the body is an example. The amount of energy necessary to fire such a neuron is a very small fraction of the total energy put out by the neuron. Thus, the motor neuron itself is the immediate source of the energy released in its firing. So, also, is the total action of the nervous system or of the whole man.

Active behavior in turn falls into two classes, termed nonpurposeful, or random, active behavior and purposeful active behavior. The latter they define as active behavior "directed to the attainment of a goal—*i.e.*, to a final condition in which the behaving object reaches a definite correlation in time or in space with respect to another object or event." They emphasize that "the purpose of voluntary act is not a matter of arbitrary interpretation but of physiological fact. When we perform a voluntary action what we select voluntarily is a specific purpose, not a specific movement. Thus, if we decide to take a glass containing water and carry it to our mouth

we do not command a certain set of muscles to contract . . . ; we merely trip the purpose and the reaction follows automatically."

Rosenblueth, Wiener, and Bigelow do not tell us in their important paper what they mean by "trip [ping] the purpose." They would be the first to admit, I believe, that without McCulloch's and Pitts' theory of universals to define the goal which is tripped, a given system, such as a robot, would have to have its purpose assigned to it by certain instructions fed into the mechanism by some purposeful being outside the system or mechanism. But if the system has the property of being an active system in Rosenblueth's, Wiener's, and Bigelow's sense, and if this active system has reverberating circuits which permit the existence of universals and the construction of postulates or proposals out of these universals which can define ends, then the system itself has the capacity to project possible goals or purposes and the capacity to trip one of these purposes rather than another.

Purposeful behavior is again divided by Rosenblueth, Wiener, and Bigelow into two types called teleological and nonteleological. The important point to note with respect to this dichotomy is that mechanisms can be constructed which exhibit either type. The key to the difference between teleological and nonteleological purposeful activity is that, in the case of nonteleological purposeful activity, "no signals from the goal . . . modify the activity of the object in the course of the behavior." They give as an example a snake which may strike at its prey with no stimulus coming from the goal after the strike has started. Teleological purposeful activity, on the other hand, occurs in any mechanism in which signals from the goal alter the behavior after it has been initiated, so that it reaches its goal. The requirement of any mechanism in order to be thus not merely goal-directed, but teleologically goal-directed, is that it possess a "negative feedback" over the goal.

Feedback may be of two kinds, positive and negative. Both kinds involve activity in a closed path. Both kinds have this in common: "some of the output . . . is returned as input." When this output which returns as input has the same direction and effect upon the system as the nonreturning input, the feedback is positive. Thus, positive feedback reinforces the input. Negative feedback, on the other hand, counteracts the input "to restrict outputs that would otherwise go beyond the goal." In other words, negative feedback means that "the behavior of an object is controlled by the margin of error at which the object stands at a given time with reference to a relatively specific goal." Thus, the modern gun is automatically controlled to hit its target. Electromagnetic waves returning to the mechanism from both the target and the projectile during flight give the error or deviation of the projectile from its intended course. This alters the input of the mechanism in such a way that the gun puts its next shell nearer the target.

It appears, therefore, that purpose, teleology, and mechanism, as Rosenblueth, Wiener, and Bigelow emphasize, are compatible rather than mutually exclusive concepts. Teleology is opposed not to mechanism but to nonteleological mechanistic systems—that is, to mechanical systems not governed in their behavior by negative feedback over the goal. Similarly, purposes are not antithetical to mechanism, but only to those whose behavior is random. Put positively, this means that a teleological system can be—and in human nervous systems it is—a mechanical system. It is a mechanical system in which the behavior of the system is controlled by a negative feedback over the goal. In fact, Rosenblueth, Wiener, and Bigelow suggest that "the main function of the cerebellum is the control of the feedback nervous mechanisms involved in purposeful motor activity."

The traditional argument of the dualists and idealists—that purposeful teleological behavior cannot be accounted for by means of scientifically verified psychology and neurology because the latter sciences give no basis for memory, universals, and purposes—and the argument of the early modern naturalists, mechanists, and their sociological followers to the effect that purposeful teleological activities and the theoretical ideas defining human goals are mere epiphenomena of no causal significance, representing mere pseudorationalizations after the fact, because again such factors are incompatible with mechanism and a scientifically verified theory of human nature, therefore apparently rest upon a common confusion and a false premise. This false premise is that teleology and mechanism are incompatible.

Rosenblueth, Wiener, and Bigelow have made it abundantly clear that this incompatibility is justified neither by logic nor by fact. When purpose and teleology are carefully defined, one finds that each represents a particular kind of mechanism and that the real dichotomies are (a) between purposeful mechanisms and mechanisms giving rise to random behavior, and (b) between teleological purposeful mechanisms which possess a negative feedback controlling their behavior and nonteleological purposeful mechanisms which do proceed toward a goal and hence have a purpose, but which do not have a negative feedback redirecting the behavior of the system on its way to its goal.

It remains to connect with the problem of our basic inquiry McCulloch's and Pitts' demonstration that

scientifically verified neurological man can know universals and Rosenblueth's, Wiener's and Bigelow's demonstration that scientifically investigated, behaving neurological man can have causally significant goals and teleologically controlled behavior toward those goals. This problem, it will be recalled, is that of the relation between ideological factors and biological factors in any culture.

Goals can be of two kinds. They may be some immediately apprehended particular, enjoyed aesthetically or used empirically to check a scientific theory of nature. But goals may also be the attempt to make the world conform to the theory of natural science, as in engineering, or to the normative theory of social science, as in education, religious conversion, new legislation, and other social reforms. The former orders the things of nature to serve man's ends. The latter attempts to alter the behavior and cultural institutions of men to fit man's normative theory. The present inquiry indicates that if the latter type of goal-seeking is to be effective, attention must be directed less upon external factors and overt behavior and more upon the preservation or removal of the traditional universals embodied in the brains of men.

In both types of goals postulated theories constructed out of McCulloch's and Pitts' universals are necessary. The manner, however, in which the negative feedback controls behavior is different in the two instances.

In the case of the deductively formulated theory of natural science, data from outside the organism coming through the sense organs of the scientist either do or do not correspond to what his deductively formulated theory, stated in terms of universals, specifies. If they do, the natural scientist, for the particular investigation in question, has reached his goal. His theory is verified. If they do not, the information fed back through the sense organs to the scientist forces him to reconstruct the postulates of his scientific theory. He may have to draw upon new reverberating circuits with their quite different universals or basic scientific concepts.

In the case, however, of a normative social theory, assuming the normative social theory to be accepted, it is this theory rather than the empirical social facts given through the senses which define the goal. Thus, the negative feedback comes from the normative theory itself to the motor neurons prescribing that the man's behavior conform to the prescriptions of the norm. It is in this manner that the censorship of personal and social norms arises and the prescriptions of an ideology for a given society operate through familial, educational, religious, commercial, and legal institutions and processes to mold *what is* in social institutions and behavior toward *what ought to be.*

Since the many reverberating circuits through the human cortex provide men with many different universals out of which to construct both their factual theories of nature and their normative theories of culture, one would expect rival hypotheses in natural science and the rival normative theories in the social sciences. That this is the case is well known. It is the presence of the latter which generates the ideological conflicts of the contemporary world.

It appears, therefore, that scientifically verified neurological theory of man makes both deductively formulated theory in the natural sciences and normative theory in the social sciences both possible and significant. One aspect of the significance of normative social theory remains to be noted. Studies of the social behavior of ants, by Theodore Schneirla and others, show that they have a remarkable social organization but a very rigid one. Norbert Wiener has emphasized that this rigidity is due to the fact that the ants have a very poor system of communications. They follow their leader by scent, *i.e.* they respond only to particulars and to particulars of but one sense organ. Human societies in the West, as the writer has noted elsewhere (*5*), radically reconstruct their social organization with the rejection of an old normative social theory and the acceptance of a new one. This is possible quickly only when a society or its leaders have reached majority agreement upon a systematic normative social theory and possess an excellent system of communications to aquaint and habituate the leaders of that society and, if possible, a majority of the people with that normative social theory.

The answer to the basic question of our inquiry may now be summarized: Cultural factors are related to biological factors in social institutions by the biologically-defined purposeful behavior of human neurological systems containing negative feedback mechanisms and the normative social theory defined in terms of the universals which are the epistemic correlates of trains of impulses in neural nets that are reverberating circuits. Because overt behavior can be tripped by impulses from reverberating circuits whose activity conforms to universals, as well as by impulses coming immediately from an external particular event, the behavior of men can be, and is, causally determined by embodiments of ideas as well as by particular environmental facts. And since the brains of men in early so-called primitive societies are provided with reverberating circuits, just as are the brains of men in so-called modern societies, it follows, though the specific universals may be different, that normative social philosophies will be significant in any culture. In short, in any culture embodied ideas defining purposes or ideals really matter.

References

1. McCULLOCH, WARREN, S. *Bull. math. Biophys.*, 1945, **7**, 89–93; "Finality and Form in Nervous Activity." James Arthur Lecture delivered May 2, 1946, at the American Museum of Natural History, New York City. (Mimeographed.)
2. McCULLOCH, WARREN S., and PITTS, WALTER. *Bull. math. Biophys.*, 1943, **5**, 115–133; 1947, **9**, 127–147.
3. DE NÓ, R. LORENTE. *Trab. Lab. Invest. Biol. Univ. Madr.*, 1922, **20**, 41–78; *Arch. Neurol. Psychiat.*, 1933, **30**, 245–291; *Stud. Rockefeller Inst. Med. Res.*, 1947, **131-132**.
4. NORTHROP, F. S. C. *The logic of the sciences and the humanities.* New York: Macmillan, 1947. Chaps. vi, vii, and viii; *The meeting of East and West.* New York: Macmillan, 1946. Chap. xii.
5. NORTHROP, F. S. C. *The meeting of East and West.* New York, Macmillan, 1946. Chaps. ii and viii.
6. ROSENBLUETH, ARTURO, WIENER, NORBERT, and BIGELOW, JULIAN. *Phil. Sci.*, 1943, **10**, 18–24.

NEWS and Notes

John N. Adkins, assistant professor of geophysics at Massachusetts Institute of Technology, has been granted a year's leave of absence to head the Geophysics Branch, Physical Sciences Division, Office of Naval Research. His activities in ONR will include directing research in meteorology, oceanography, and earth sciences being carried on under contract in leading university, government, and industrial laboratories throughout the country. The Geophysics Branch also directs the scientific aspects of various expeditions. Dr. Adkins succeeds **Roger R. Revelle,** who will return to the Scripps Institution of Oceanography as associate director after a leave of absence from that institution.

C. Merrill Whorton and **Frank C. Womack** will join the faculty of the School of Medicine, Louisiana State University, as assistant professors of pathology on July 1. Dr. Whorton is at present associated with the Mallory Institute of Pathology, Boston City Hospital, and is on the staff of Tufts Medical College, and Dr. Womack is an instructor in pathology at Vanderbilt University School of Medicine.

Carroll L. Mann, who has headed the Department of Civil Engineering at North Carolina State College since 1916, will retire on June 30.

G. B. MacDonald will retire as head of the Forestry Department, Iowa State College, on July 1 but will continue as professor in the Department. The chairmanship will be taken over by **George B. Hartman,** a 1917 graduate in forestry from Iowa State College, who has been associated with the Long Bell Lumber Company in Louisiana.

Thomas C. Poulter, associate director of the Armour Research Foundation, will join the staff of the Stanford Research Institute in a similar capacity later this year. In addition to the research he has done in many scientific fields, he is a well-known Antarctic explorer.

Carl Nielsen, associate director of research at Abbott Laboratories, North Chicago, Illinois, has been made a knight of the Order of Dannebrog by Frederik IX, King of Denmark, in recognition of his work in promoting closer relationships between Denmark and the United States, especially in the scientific and pharmaceutical fields.

Robert E. Dickinson and **Henry M. Kendall** have been appointed full professors in the Department of Geography, Syracuse University. Dr. Dickinson, formerly of the University of London, will have charge of work in political geography, the development of geographic thought, and the geography of Europe, while Dr. Kendall, formerly of Amherst, will be responsible for introductory work in geography and climatology.

Donald M. Hester, former assistant professor of mathematics at the New Mexico School of Mines, has joined the faculty of the Northeast Missouri State College, Maryville.

Roger M. Herriott, associate in general physiology at the Rockefeller Institute for Medical Research, Princeton, New Jersey, has been appointed professor of biochemistry at the Johns Hopkins University School of Hygiene and Public Health, effective July 1. Dr. Herriott will succeed **Reginald M. Archibald,** who has accepted a position at the Rockefeller Institute.

Robert J. Lowry, assistant professor of botany at Michigan State College, has been appointed to a similar post at the University of Michigan for the academic year 1948–49.

Sergio De Benedetti, of the Clinton Laboratories, Oak Ridge, Tennessee, has been appointed associate professor of physics at Washington University, St. Louis.

John Phillips, head of the Botany Department, Witwatersrand University, Union of South Africa, has been named director of the British Overseas Food Corporation, which is to handle all food production developments in the British Colonial Empire. An authority on South African soil conservation, Prof. Phillips will direct Colonial agricultural policy and research. He will take up his new post next November.

Lawrence H. Aller, assistant professor of astronomy at Indiana University, has been appointed associate professor of astronomy at the University of Michigan beginning August 1.

Visitors to U.S.

N. P. Allen, superintendent of the Metallurgy Division, National Physical Laboratory, Teddington, England, arrived in this country on April 21 for a two-month visit.

D. J. Watson and his wife, **M. A. Watson,** both members of the staff of the Rothamsted Experimental Station, England, after spending several months in Australia, have arrived here and are now visiting various research centers. They are traveling under a fellowship awarded them by the Ministry of Agriculture.

H. A. McKenzie, research officer in the Division of Food Preservation, Australian Council for Scientific and Industrial Research, is spending approximately 9 months in physical chemistry research at the Frick Chemical Laboratory, Princeton University.

Colleges and Universities

A fully-equipped German Diesel engine research laboratory, valued at more than $1,000,000, is soon to be transplanted to the campus of Oklahoma A & M College, according to an announcement made by John W. Studebaker, Commissioner of Education. Location of the former Klockner-Humboldt-Deutz laboratory at Stillwater will provide the College with one of the two largest Diesel engine research centers in this country, the other center being at Pennsylvania State College. Oklahoma A & M's Division of Engineering is to be replaced by the Oklahoma Institute of Technology, established as a result of allocation of the laboratory.

The KHD laboratory, formerly located at Oberursel, Germany, was assigned to the United States by the Joint Chiefs of Staff shortly after VE-Day, and the donation to Oklahoma A & M was made possible through a joint allocation of OTS, Department of Commerce, and the Office of Education, FSA. Oklahoma was selected from 114 colleges not only because of its location in the interior of the country, but also because of its location near the oil industry, the availability of building space, and the availability of funds to defray the large annual expense of conducting this type of research.

Through the Visiting Scholars Program of the University Center of Georgia several persons have recently served as advisers in academic programs of the institutions in the Center as well as delivering formal lectures. Among those who took part in the February program were Merle Curti, professor of history, University of Wisconsin, who lectured at Emory University and Agnes Scott College on "The American Mind in Postwar Eras"; Thomas Munro, curator of the Cleveland Museum, who discussed "The Arts in Modern Life" at Emory and the University of Georgia; Dael Wolfle, executive secretary of the American Psychological Association, who conducted a series of seminars, conferences, and lectures for the Departments of Psychology at the University of Georgia, Agnes Scott College, Emory University, and the Georgia School of Technology; and William F. Windle, chairman of the Department of Anatomy, University of Pennsylvania Medical School, who lectured on various aspects of embryology at Emory University, the University of Georgia Medical School, and Grady Memorial Hospital in Atlanta. These visits are made possible by grants from the Committee on Visiting Scholars and are shared in by as many institutions in the Center as possible.

Summer Programs

A course on Catalysis in Organic Chemistry will be offered June 25–August 28 by Northwestern University in the recently dedicated Teaching Unit of the Ipatieff High Pressure and Catalytic Laboratory. The course will cover principles of catalysis, hydrogenation, dehydrogenation, oxidation, isomerization, polymerization, alkylation, catalytic cracking, hydration, dehydration, and condensation. In the laboratory, which is equipped with the latest type of apparatus especially designed for instruction in catalytic techniques, each student will have an opportunity to carry out catalytic reactions under pressure and at atmospheric pressure. Some of the experiments will cover methods of handling gaseous substances. A laboratory manual has been prepared for this course. Herman Pines, who is to give the course, has been a close collaborator of Prof. Ipatieff for the last 18 years. Further information may be obtained by writing to: Director, Summer Session, Northwestern University, Evanston, Illinois.

The Biological Laboratory, Cold Spring Harbor, New York, in an effort to stimulate interest in research with bacteriophages, is again offering a summer course for research workers. The course, to be given by Mark H. Adams, of New York University, is designed to acquaint scientists with some of the techniques used in research with bacterial viruses and with the recent results of such work. It will be held from June 28 to July 17.

A Symposium on Theoretical and Nuclear Physics, extending from June 28 to August 11, has been announced at the University of Michigan. Visiting lecturers include H. B. G. Casimir, Philips Research Laboratory, Eindhoven, who will be in residence throughout the session and who will present "Theoretical Aspects of Low-Temperature Physics"; Julian Schwinger, Harvard University, whose topic will be "Recent Developments in Quantum Electrodynamics"; E. M. McMillan, University of California, who will deal with "Recent Experiments in High-Energy Physics"; and Martin Deutsch, Massachusetts Institute of Technology, whose subject will be "Selected Topics in Nuclear Spectroscopy." Semi-weekly seminars will also be arranged.

There will be no fees for visitors holding the doctoral degree. A prospectus and further information may be obtained from the Department of Physics, University of Michigan, Ann Arbor.

The Tissue Culture Commission is sponsoring a four-week course dealing with the principles, methods, and applications of tissue culture. The course will be given under the direction of Raymond C. Parker at the Connaught Medical Research Laboratories, University of Toronto, from July 5 to July 30. Instruction will include demonstrations and first-hand practical experience for the student in all major current procedures, as well as daily lectures by visiting investigators experienced in various fields.

Applications should be sent to Margaret R. Murray, secretary of the Commission, whose address is 630 West 168th Street, New York City 32. These should include information relative to the present position of the applicant, his academic and other training pertinent to the undertaking, and the general nature of the project for which he wishes to use the techniques. The number admitted to the course will of necessity be limited. To be considered, applications must reach the secretary by May 15; applicants will be notified concerning their acceptance by June 1. The fee for the

course will be $50.00, payable upon admission. Housing accommodations in Toronto will be available at reasonable rates at the University dormitories.

Meetings and Elections

The American Institute of Biological Sciences, associated with the Division of Biology and Agriculture, National Research Council, with headquarters at 2101 Constitution Avenue, Washington, D. C., is assisting in the arrangements for the annual meetings of biological societies meeting in Washington, September 10–13, prior to the centennial meeting of the American Association for the Advancement of Science.

The participating societies are the Botanical Society of America, the American Society of Zoologists, the Genetics Society, the American Society of Plant Taxonomists, and the Mycological Society of America. The Limnological Society and the Ecological Society plan to hold their meetings and will be housed at the University of Maryland. Tentative plans to meet at the same time have also been made for the Phycological Society of America and the American Microscopical Society.

The American Institute of Nutrition, at the Atlantic City Meeting of the Federation of American Societies for Experimental Biology, March 14–19, elected the following officers for 1948–49: E. M. Nelson, president; C. G. King, vice-president; N. R. Ellis, treasurer; and J. H. Roe, secretary.

The American Society for X-Ray and Electron Diffraction and the **Crystallographic Society of America,** meeting in joint scientific sessions for the first time, were the guests of Yale University March 31 through April 3. The meetings, at which about 60 papers were presented, were attended by 190 crystallographers and featured a symposium on the structures of organic crystals.

Among the new developments in computation methods designed to facilitate the laborious calculations required for the determination of the positions of atoms in complex structures is the production of an oscilloscope-screen image of an accurate contour map of electron densities or "Patterson functions," described by R. Pepinsky, of Alabama Polytechnic Institute. Prof. Pepinsky's paper was interrupted by a burst of spontaneous applause when the contour-map image was shown.

W. H. Zachariasen, of the Argonne National Laboratory and the University of Chicago, described the crystal chemistry of a group of compounds containing the elements from actinium (89) through americium (95). The structures of 96 of these have been completely determined, some of them by Rose C. L. Mooney, and partial structural determination has been achieved for 46 additional compounds. The crystal structures of the elements have also been determined, but they are not yet available for publication. This work necessitated exceptionally refined X-ray diffraction methods since the samples available were very small, some of them weighing less than 10μg.

Papers on the structures of silicate crystals and their interrelations were presented by W. J. Gruner, of the University of Minnesota, retiring president of the Crystallographic Society of America, and by M. J. Buerger, of the Massachusetts Institute of Technology.

B. T. Matthias, of the Bell Telephone Laboratories, in a paper vividly illustrated by colored photomicrographs, described the ferroelectric behavior of single crystals of barium titanate, reporting the results of work done by him at the Massachusetts Institute of Technology. This substance, which has a dielectric constant 300 times that of quartz, occurs in a variety of crystal types whose interrelations are as yet only imperfectly understood.

Among the instruments featured in the instrumentation session was an improved Geiger counter spectrometer with extended angular range for sensitively detecting X-rays reflected at high angles, described by E. A. Hamacher and W. Parrish, of the Philips Laboratories. A double curved-crystal monochromator, giving high-intensity radiation with a minimum of parasitic scattering, was developed by A. Guinier and G. Fournet of the Laboratoire d'Essais des Arts et Métiers in Paris for the study of low-angle scattering of X-rays from crystalline substances. Their paper was read, in their absence, by I. Fankuchen, of the Brooklyn Polytechnic Institute. (ELIZABETH A. WOOD.)

(The officers of ASXRED are pictured on the cover of this issue. They are, left to right: C. S. Barrett, Institute for the Study of Metals, University of Chicago, counselor; A. L. Patterson, Bryn Mawr College, president; E. A. Wood, Bell Telephone Laboratories, secretary; and C. C. Murdock, Cornell University, treasurer. P. P. Debye, of Cornell University, who is vice-president, was unable to attend the meeting.)

The American Society for Pharmacology and Experimental Therapeutics, at its annual business meeting in Atlantic City on March 16, elected the following officers: Carl A. Dragstedt, Northwestern University Medical School, Chicago, president; H. B. Van Dyke, Columbia University, vice-president; H. B. Haag, Medical College of Virginia, Richmond, secretary; K. K. Chen, Lilly Research Laboratories, Indianapolis, treasurer; and Arthur C. DeGraff, New York University College of Medicine, Robert A. Woodbury, University of Tennessee, Memphis, and Gordon A. Alles, 770 South Arroyo Parkway, Pasadena, California, councilors.

NRC News

Word has been received by the National Research Council that the Royal Society of New Zealand, in cooperation with the New Zealand scientists and the Government of New Zealand, is actively engaged in developing plans for holding the 7th Pacific Science Congress in 1949. The meetings are scheduled for Auckland from February 2 to 8 and for Christchurch from February 16 to 22. Excursions in the North Island are scheduled for February 9 to 15 and in the South Island after the 22nd.

The 6th Pacific Science Congress was held in California in 1939 and the 7th Congress was projected for the Philippines in 1943. Plans for holding the latter Congress were changed

at the request of the Philippine Government on account of the extensive war damage to their scientific installations. After consultation with member countries, the Council of the Pacific Science Association approved the invitation of New Zealand to be the host country for the 7th Congress. The 6 previous Congresses have been held in Honolulu, Australia, Japan, the Netherlands East Indies, Canada, and the United States.

The Congress will be organized in 10 Divisions, within which there will be a varying number of sections. The Divisions cover the fields of Geophysics and Geology, Meteorology, Oceanography and Marine Biology, Zoology, Botany, Soil Resources and Agriculture, Anthropology, Public Health and Nutrition, Social Sciences and related sciences in so far as the Pacific Ocean region is concerned.

The Pacific Science Board of the NRC will be glad to hear from American scientists who expect to attend the Congress in New Zealand.

Deaths

R. Bruce Horsfall, 80, well-known illustrator of scientific articles, books, and museum habitat groups, died March 24 at Monmouth Memorial Hospital, Long Branch, New Jersey. As recently as two years ago he was actively engaged in painting backgrounds for displays in the Rutgers University Geological Museum, to which he recently donated about 1,000 paintings and drawings of wildlife and scenery.

Howard L. Kingsley, 55, professor of educational psychology at Boston University, died April 7.

Thomas S. Gates, 75, president of the American Philosophical Society and chairman and former president of the University of Pennsylvania, died suddenly April 8 at his summer home on Cape Cod, after a long career of leadership and public service.

Rupert Blue, 80, Surgeon General of the U. S. Public Health Service from 1912 to 1920 and a past president of the American Medical Association, died April 12 at Roper Hospital, Charleston, South Carolina.

E. Monroe Bailey, 68, head of the Analytical Chemistry Department at the Connecticut Agricultural Experiment Station for 28 years prior to his retirement in September 1945, died in New Haven April 13.

The Robert H. Goddard Rocket Exhibit opened April 22 for a 3-month showing at the American Museum of Natural History in New York. Prior to his death in 1945, Dr. Goddard had been engaged in rocket research for 35 years, earlier as a professor of physics at Clark University and during the war as a U. S. Navy investigator at Roswell, New Mexico. Among the items in the collection will be found a 22-foot pressure-type liquid-fuel rocket, 18 inches in diameter; a smaller pump-type liquid-fuel rocket; a number of dry powder rocket projectiles; and 5 different types of rocket motor heads which Dr. Goddard developed in search for an efficient fuel feed. A special feature of the exhibit is a revised version of the world's first liquid-fuel rocket, which was fired for 2½ seconds and rose in a high trajectory, traveling a distance of 184 feet. Its average speed was 60 mph, and its fuels were liquid oxygen and gasoline. The principles of rockets and jet propulsion will be traced historically from 1909 to the time of Dr. Goddard's death through the use of pictures and actual samples.

The exhibit is sponsored by the Daniel and Florence Guggenheim Foundation, which had contributed support to Dr. Goddard's work from 1930 to 1945.

P. D. Nieucokoop, of the Zoological Laboratory of the Rijks-Universiteit, Janskerkhof 3, Utrecht, Holland, would be grateful for reprints in the field of experimental embryology, especially concerning the central nervous system.

The American Society of Mechanical Engineers, under the sponsorship of the Engineers Joint Council, early last month published *The engineering societies yearbook, 1948,* the first of a planned periodical series on the purposes, activities, membership, policies, and new developments of all engineering societies, clubs, and councils. Thirty-five Canadian and 275 U. S. societies and 8 international organizations are described. Information is also given on student branches of national societies. The 5 societies sponsoring the *Yearbook* (AIEE, AIME, ASCE, ASME, and AIChE) had a total of 119,588 members in the fall of 1947; of these, 22,517 were student members. A combined membership of 337,000 is estimated for 1950.

The *Yearbook* is priced at $3.00, and copies are available from the ASME, 29 West 39th Street, New York City 18.

Make Plans for—

Kansas Academy of Science, 80th annual meeting, April 29–May 1, Pittsburg, Kansas.

Society of American Bacteriologists, Texas Branch, April 30–May 1, Baylor Medical School, Houston, Texas.

American Section, International Scientific Radio Union, joint meeting with **Institute of Radio Engineers,** May 3–5, Washington, D. C.

Association of American Physicians, May 4–5, Chalfonte-Haddon Hall, Atlantic City, New Jersey.

Ohio Academy of Science, May 6–8, University of Toledo.

American Institute of Chemists, Annual Meeting and Silver Anniversary commemoration, May 7, Hotel Pennsylvania, New York City.

Society of American Bacteriologists, May 10–14, Nicollet Hotel, Minneapolis, Minnesota.

American Psychiatric Association, May 17–20, Statler Hotel, Washington, D. C.

Conference on Hemoglobin, June 15–18, Cambridge, England.

American Medical Association, annual session, June 21–25, Chicago, Illinois.

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AAAS
Centennial Celebration
Washington, D. C.
September 13–17, 1948

★ ★

Comments and Communications

Effect of Anoxia and Cytochrome C on Readily Hydrolyzable Phosphate of Rat Tissues

Proger, *et al.* (*Bull. New Engl. med. Center*, 1945, 7, 1, 149; 1947, 9, 211; *J. biol. Chem.*, 1945, 160, 233; *J. clin. Invest.*, 1945, 24, 864; *Science*, 1946, 104, 389; 1947, 106, 367) have found that in the presence of anoxia the readily hydrolyzable phosphate (adenosine triphosphate) of tissue decreases, but the previous administration of cytochrome C prevents such a decrease. Several workers have confirmed the decrease in the presence of anoxia, but Scheinberg and Michel (*J. biol. Chem.*, 1947, 169, 277; *Science*, 1947, 105, 365) and, more recently, Stadie and Marsh (*J. clin. Invest.*, 1947, 26, 899) found no significant effect of cytochrome C.

According to Proger, the low concentration of the cytochrome in tissue may be the limiting factor in the rate of oxygen utilization; hence, the administration of cytochrome should permit an increased utilization in the presence of a deficient oxygen supply. Stadie and Marsh have presented data on the basis of which they question the theoretical validity of Proger's hypothesis. Christensen and Pearson (*J. clin. Invest.*, 1947, 26, 1046) have found no increase in oxygen uptake by heart and kidney slices equilibrated at oxygen tensions of 2.5–100% when cytochrome was added. Potter (*Science*, 1947, 106, 342) has also criticized the hypothesis, but has offered no additional data.

The data Proger published in 1945 show a statistically significant effect of injected cytochrome C. Although Scheinberg and Michel and Stadie and Marsh could not confirm this finding, Proger has recently repeated his experiments and confirmed his earlier results.

In view of the importance of establishing whether or not cytochrome C can prevent the anoxia-induced decrease in readily hydrolyzable phosphate, it seems of importance to add to the literature the data obtained in this laboratory.

Albino rats weighing 150–230 gm, maintained on Purina Laboratory Chow, were used. They were divided by weight and sex into 11 groups of 3 each; each group was kept in a separate cage and used as the basis of one experiment. All animals used were females with the exception of two groups (6 animals).

The cytochrome C was prepared according to the method of Keilin and Hartree (*Proc. roy. Soc. Lond.*, 1937, **B122**, 298) and standardized spectroscopically and by analysis for iron. The iron content was 0.34%.

After being anesthetized by ether, two rats were injected intravenously in the tail with 0.7 ml of isotonic saline, and the third animal was injected with 0.7 ml of a solution of cytochrome C containing 8 mg/ml—a total of 5.6 mg of cytochrome. Ten minutes after injection, the cytochrome-injected rat and one saline-injected rat were put in a desiccator through which a mixture of 3% oxygen and 97% nitrogen was passed at a rate of 10 liters/min. After 8 min, these rats were decapitated and the heart and right kidney dropped into an absolute alcohol and solid carbon dioxide bath at −70°. Thirty to 50 sec were required for this operation. The other saline-injected animal (control) was left in the open air and similarly killed 18 min after injection.

The organs were then weighed and homogenized in 25 ml of 5% trichloroacetic acid in a Waring blender. The solution was filtered, and 9 ml was mixed with 1 ml of 10 *N* sulfuric acid and hydrolyzed at 100° for 7 min.

Phosphate determinations were done before and after hydrolysis by the method of Fiske and Subbarow (*J. biol. Chem.*, 1925, 66, 375), using a Coleman Junior Spectrophotometer at 540 mμ. All solutions were adjusted to contain 0.3 *N* sulfuric acid and 4% trichloroacetic acid in the 10 ml of solution to be read.

TABLE 1

EFFECTS OF ANOXIA AND CYTOCHROME C ON READILY HYDROLYZABLE PHOSPHATE*

Experiment	Kidney			Heart		
	Control	Anoxia plus saline	Anoxia plus cytochrome C	Control	Anoxia plus saline	Anoxia plus cytochrome C
1	7.3	3.3	7.2	14.2	10.8	11.4
2	5.8	4.8	4.6	13.1	5.8	5.3
3	7.3	7.0	2.8	10.9	10.2	9.9
4	12.9	5.1	4.8	14.5	10.5	7.5
5	9.3	6.8	6.6	9.1	8.9	10.8
6	5.0	6.9	5.9	8.3	9.4	11.7
7	12.5	5.6	7.0	18.2	11.8	10.9
8	9.9	6.7	7.7	15.3	10.4	12.6
9	10.2	5.5	6.3	18.4	13.8	15.8
10	15.5	8.8	8.0	20.3	15.5	14.1
11	9.4	12.3	6.3	10.9	8.7	12.5
Mean	9.6	6.6	6.1	13.9	10.5	11.1

* Data expressed as mg of phosphate/100 gm of wet tissue.

The data are given in Table 1. No effect of cytochrome C on the readily hydrolyzable phosphate was found. Applying the *t* test of Fisher (*Statistical methods for research workers*, 9th ed., 1944) to the data, the decrease in hydrolyzable phosphate in anoxic animals was found to be highly significant ($P < 0.01$), but the difference between the cytochrome-treated and non-cytochrome-treated anoxic animals was not significant.

Conclusions: (1) Anoxia reduces the amount of readily hydrolyzable phosphate in rat kidney and heart. (2) Previous intravenous injection of cytochrome C in doses of 5.6 mg/animal has no effect in preventing this reduction.

WADE N. MILLER, PEARL ANDERSON, and ALBERT DORFMAN

Army Medical Department Research and Graduate School, Washington, D. C.

Sympathin E and Nor-Adrenaline

The demonstration of a substance in extracts of 'adrenergic' nerves which conforms in biological and chemical respects with nor-adrenaline (U. S. v. Euler. *Acta physiol. Scand.*, 1946, **12**, 73; *J. Physiol.*, 1946, **105**, 38; 1948 data, to be published) has actualized the question as to the relations between this substance and the sympathin E of Cannon and Rosenblueth (*Autonomic neuro-effector systems.* New York: Macmillan, 1937). A contribution to this discussion was recently published in *Science* (November 28, 1947, p. 520) by Marrazzi and Marrazzi.

The conception of an excitatory sympathin E was primarily based on the fundamental discovery that only excitatory effects were obtained on stimulation of certain sympathetic nerves. Since nor-adrenaline is a substance possessing similar properties, being predominantly excitatory in its actions (G. Barger and H. H. Dale. *J. Physiol.*, 1910, **41**, 19), it has been repeatedly suggested that it might be identical with the postulated sympathin E (Z. M. Bacq. *Ann. Physiol. Physicochim. biol.*, 1934, 10, 467; U. S. v. Euler. *J. Physiol.*, 1946, **105**, 38; C. M. Greer, *et al.* *J. Pharm. exp. Therap.*, 1937, **60**, 108; 1938, 62, 189; R. L. Stehle and H. C. Ellsworth. *J. Pharm. exp. Therap.*, 1937, **59**, 114).

The conclusion reached by the Marrazzis that nor-adrenaline cannot be identical with sympathin E opens some questions of principal interest which may invite some discussion.

Obviously, the nor-adrenaline shown to be present in the nerves themselves cannot be the sympathin E of Cannon and Rosenblueth, in the meaning of these authors, for the following two reasons:

(1) It is present in, and can be liberated from, the adrenergic nerves themselves (U. S. v. Euler. 1948 data, to be published) and need not be formed secondarily in the effectors, as is assumed for sympathin E.

(2) It is predominantly but not exclusively excitatory (G. Barger and H. H. Dale. *J. Physiol.*, 1910, **41**, 19; U. S. v. Euler. *Acta physiol. Scand.*, 1946, **12**, 73; G. B. West. *J. Physiol.*, 1947, **106**, 418).

It should be observed, however, that sympathin E in its original meaning has never been prepared nor have its assumed properties been controlled in detail. The possibility that the active substance responsible for the observed actions is liberated directly from the nerves is hard to exclude, and, with regard to its purely excitatory action, it is easy to imagine that a weak inhibitory action could have been overlooked. This is illustrated by Fig. 1, which shows the effects of an extract from splenic nerves of cattle on the blood pressure and the uterus *in vivo* of the cat. With a moderate dose, corresponding to 1 μg of 1-nor-adrenaline (kindly placed at my disposal by M. L. Tainter), no action could be detected on the uterus, whereas larger doses evoked a small but definite inhibitory action.

We believe, therefore, that the actions described y Cannon and Rosenblueth and attributed to sympathin E are due to the substance shown to be present in adrenergic nerves, having the properties of nor-adrenaline. On the other hand, since there is so far no convincing evidence for the presence of a sympathin E different from nor-adrenaline, this former term should preferably be dropped as inadequate in the strict sense.

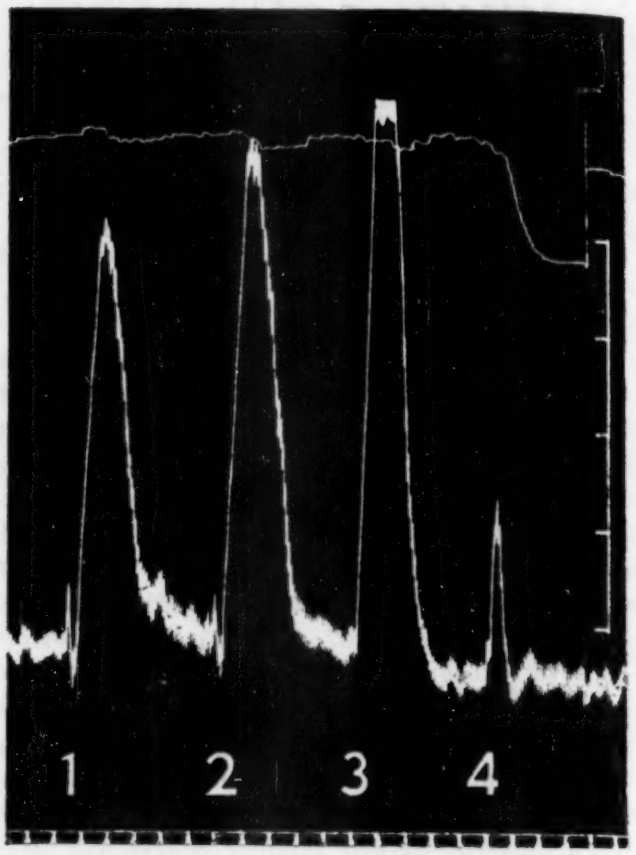

FIG. 1. Cat, chloralose. Gynergen, 0.1 mg/kg i.v.; atropine, 1 mg/kg s.c.; antergan, 5 mg/kg i.m. + 1 mg/kg i.v. Upper curve—movements of uterus; lower curve—blood pressure: (1) extract of 0.2 gm of splenic nerves, cattle; (2) extract of 0.3 gm of splenic nerves, cattle; (3) 3 μg of 1-nor-adrenaline hydrochloride; (4) 2 μg of 1-adrenaline hydrochloride. Time, 30 sec. Ordinate, B.P. 120–200 mm Hg.

The question whether adrenaline is liberated from certain kinds of adrenergic axones is not thoroughly clear, though the results of Gaddum and his co-workers (*J. Physiol.*, 1938, **94**, 87; 1939, **96**, 104, 385) strongly suggest such a possibility. If the term sympathin is taken to denominate any active sympathomimetic ergone liberated from 'adrenergic' axones, as recently proposed by Bacq and Fischer (*Arch. int. Physiol.*, 1947, **55**, 73), it seems more satisfactory to use the distinctions sympathin N and sympathin A, which would then signify the transmitter having the properties of nor-adrenaline and adrenaline, respectively. This nomenclature would have the additional advantage of leaving place for any new kinds of similar transmitters.

U. S. v. EULER

University School of Medicine (Karolinska Institutet), Stockholm

TECHNICAL PAPERS

Essentiality of Calcium in the Nutrition of Fungi

ROBERT A. STEINBERG

Plant Industry Station,
U. S. Department of Agriculture, Beltsville, Maryland

Much of the data on the calcium and other mineral requirements of the fungi are, as is well known, of doubtful value. Compounds of unknown purity in nutrient solutions of haphazard and unstudied proportions and concentrations are the rule and not the exception. Conclusions concerning indispensability of chemical elements, based on growth levels well within the range of extreme starvation, have been made and even generally accepted. Nevertheless, it would appear certain that one fungus, *Aspergillus niger* van Tiegh., can attain maximum growth and development with a minimal salt solution containing only very faint spectroscopic traces of calcium (*1, 3*).

TABLE 1

EFFECT OF OMISSION OF CALCIUM ON GROWTH OF FUNGI

Fungus	Control (mg)	Yield without calcium (%)
Aspergillus niger van Tiegh.	1,250.0	100.0
Rhizoctonia solani Kuehn	1,215.1	14.3
Sclerotium rolfsii Sacc.	1,082.3	49.5
Cercospora nicotianae Ell. & Ev.	1,380.2	90.1*
Fusarium oxysporum Schlecht var. *nicotianae* J. Johnson	823.3	100.0
Pythium irregulare Buis.	459.0	60.1*
Thielaviopsis basicola (Berk. & Br.) Ferr.	364.2	82.0*

* Asparagine of unknown purity.

Studies by the writer on the nutrient requirements of the fungi pathogenic to the tobacco plant have been under way for some time under conditions identical with those employed with *Aspergillus.* The experimental technique includes the exclusive use of quartzware, triply distilled water, sucrose of 0.00087% ash, and either selected reagent grade or spectroscopically pure salts and spectroscopically pure micronutrients. All salts (NH_4NO_3, K_2HPO_4, $MgSO_4 \cdot 7H_2O$, asparagine) were used in minimal quantities sufficient for maximum yields with 50 ml of a 5% sucrose solution. The macronutrients therefore included were C, H, O, N, K, P, Mg, and S. Micronutrients comprised Fe, Zn, Cu, Mn, Mo, and Ga, also in minimal quantity sufficient for maximum yield.

Since subsidiary problems that have arisen and other factors may delay publication perhaps indefinitely, it was considered desirable to make a preliminary report of the results so far obtained with calcium. These are briefly summarized in Table 1.

Omission of calcium from the solution caused maximum decreases in yield with *Rhizoctonia.* Of a total of 15 trace elements investigated, none could replace calcium in the nutrition of *Rhizoctonia.* In addition, only strontium, but not barium, gave partial replacement (*4*) of calcium sufficing for approximately 50% growth. The otherwise spectroscopically pure strontium chloride used contained a very slight trace of calcium.

The quantities of calcium required for maximum yields with these fungi ranged from 2 to 6 ppm, whereas the minimum quantity of magnesium needed (*Rhizoctonia*) was 14 ppm. Calcium, therefore, might be considered a micronutrient instead of a macronutrient in the nutrition of fungi, except that it would appear more logical to continue to limit use of "micronutrient" only to those trace elements discovered to be biologically essential for growth.

According to these data, the causes for pathogenicity would appear to be dissociated from mineral requirements. *Rhizoctonia* and *Fusarium* are plant parasites of widespread occurrence, but the former appears to require calcium, whereas the latter does not. *Aspergillus,* a typical saprophyte, behaves like *Fusarium* in this respect. In other respects the mineral requirements of these fungi are almost identical.

As will be noted four of these fungi gave yields (dry weight, 103—5° C) ranging from about 50 to 55% of the sucrose supplied. This is also the approximate percentage yield of yeast in aerated culture. It is probable, therefore, that utilization factors of this magnitude are indicative of optimum nutrition, and lower values, of starvation and possible abnormality.

Since it is generally accepted that cellular nutrition is basically quite similar in all types of organisms, these results again lend emphasis to a question of fundamental importance. Can the protoplasm of organisms able to dispense with calcium, cobalt, molybdenum, chlorine, iodine, or boron carry out all basic biochemical reactions identically? That is, are these "optional" indispensable chemical elements employed only for the purpose of supplementing the generally required essential elements in the fundamental reactions of protoplasm, or are these particular elements associated with new biochemical reactions? It is not impossible, however, that a marked increase (*i.e.* to 1 part per billion) in the present level of purity in nutrition studies will reveal a greater degree of uniformity (*2*) in mineral requirements for all organisms.

References

1. STEINBERG, ROBERT A. *J. agric. Res.,* 1937, **55**, 891–902.
2. STEINBERG, ROBERT A. *J. agric. Res.,* 1938, **57**, 851–858.
3. STEINBERG, ROBERT A. *Plant Physiol.,* 1945, **20**, 600–608.
4. STEINBERG, ROBERT A. *Amer. J. Bot.,* 1946, **33**, 210–214.

Prevention of Trichobezoar in the Cotton Rat, *Sigmodon hispidus hispidus*[1]

S. R. Howell, C. A. Schlack, C. M. McCay, and B. L. Taylor[2]

Until 1939 the cotton rat, *Sigmodon hispidus hispidus*, was not commonly employed in experimental work. However, since the studies of Armstrong (*1*), many investigators have used this rodent in biological studies (*3, 5–9*). In spite of its increasing popularity in experimental work, a review of the literature reveals no mention of trichobezoar formation in this animal.

In our studies of experimental caries in the cotton rat (*4*) the mortality rate was found to be about 40% during a 14-week experimental period. Autopsy of those animals dying prior to the termination of the experiment consistently revealed trichobezoar formation. It occurred to one of us (C. M. McC.) that the addition of cellulose to the diet might prevent this condition.

One group of 51 weanling cotton rats (Group I) received the basic sugar caries-producing synthetic diet of Shaw, *et al.* (*8*), and a second group of 15 weanling cotton rats (Group II) received the same diet with the addition of 10% by weight of finely divided cellulose. The latter was so distributed throughout the diet that it was impossible for the rats to separate and reject it.

Group I was divided into three equal subgroups in such a manner that a rat in subgroup A had a litter mate in subgroups B and C. Group II was similarly divided.

TABLE 1

Comparison of Weights Gained and Incidence of Trichobezoars Between Group I, Receiving No Cellulose, and Group II, Receiving 10% Cellulose in the Diet*

	Group I—Caries diet					Group II—Caries diet + 10% cellulose				
	Total No. of rats	Total No. of litters	Total wt. gained (gm)	Mean wt. gained (gm)	Incidence of tricho-bezoars	Total No. of rats	Total No. of litters	Total wt. gained (gm)	Mean wt. gained (gm)	Incidence of tricho-bezoars
Subgroup A—all rats; distilled drinking water only	17	12	639	37.6	17+	5	4	412	82.4	5-
Subgroup B—all rats; Group I = .02% potassium oxalate in distilled drinking water Group II = .0002% potassium oxalate in distilled drinking water	17	12	734	43.2	17+	5	4	395	79.0	5-
Subgroup C—all rats; Group I = .22% potassium oxalate in distilled drinking water Group II = .002% potassium oxalate in distilled drinking water	17	12	743	43.7	17+	5	4	396	79.2	5-
Subgroup A—only those rats living 14 weeks; distilled drinking water	9	9	367	40.8	9+	5	4	412	82.4	5-

t value at 1% level = 3.55—$P < .01$ ∴ difference is significant.

*Difference in weights gained of rats surviving 14 weeks in subgroups IA and IIA was tested for significance.

One-third of Group I and Group II (control subgroups IA and IIA) drank distilled water, while to the drinking water of the remaining two-thirds (subgroups IB,IC and IIB,IIC) varying amounts of potassium oxalate were added. This regime was maintained for a period of 14 weeks.

Whereas the above method of procedure was originally designed to determine the role of oxalates in rat dental caries, the same animals were used concurrently to observe the effects of cellulose on trichobezoar formation.

The environmental conditions of both groups were identical, and the temperature and humidity of the animal laboratory were kept at a constant level at all times.

Rats dying during the course of the experiment were weighed and autopsied and the data recorded. With the termination of the experimental period all surviving rats

[1] Project X–418, Report No. 8, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland. The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.

[2] Commander, DC, USN; Commander, DC, USN; professor of nutrition, Cornell University; and CPhM, USN, respectively.

The authors are indebted to V. J. Berzinskas, PhMl, USN, for his work in the care and feeding of the rodents and in postmortem examination, and to Dr. John P. Flynn and L. J. Gerende, CPhM, USN, for their valuable assistance in the statistical analysis of the data.

were killed and were similarly weighed, autopsied, and examined for trichobezoar.

Of the rats in Group I receiving the basic sugar caries-producing synthetic diet, a total of 21 died before the end of the 14-week period, giving a mortality rate of about 40%. Postmortem examination of all Group I rodents consistently showed trichobezoar formation. The size of the trichobezoars varied somewhat, but in those rats that died during the experiment they were apparently of sufficient size to interfere effectively with gastric emptying. These trichobezoars were at least as large as one-half of the stomach volume, and some were so large as to fill the stomach completely. Multiple trichobezoars were found in several of the rats, but no more than three were found in any one animal. All other organs appeared normal on gross examination.

Of the Group II animals receiving the basic sugar caries-producing diet with the addition of 10% cellulose, all lived the full 14 weeks and appeared quite normal in contrast to the moribund appearance of the previous group. Autopsy of these rats showed no evidence of trichobezoar formation, and all organs and tissues were grossly normal.

Comparison of the weight gains of the rats (Table 1) indicates the marked difference between the two major groups. This difference was shown to be significant by comparison of subgroups IA and IIA according to accepted statistical methods (*2*). Since an analysis of the weight gains of the rats showed no significant difference between A and B, A and C, and B and C within both major groups, it was felt that Groups I and II, as a whole, could logically be compared for weight gains by analysis of the control subgroups IA and IIA. As seen in Table 1, only those rats of Group I which survived the full 14 weeks were used for evaluation. The t value between the control subgroups demonstrates that there is a significant difference in the weights gained, indicating that the cellulose may have been the responsible factor.

The possible effects of the oxalates on trichobezoar formation may be discounted by comparison of trichobezoar distribution among the subgroups of major groups I and II (Table 1). Since the trichobezoars were distributed equally throughout the control rats and rats receiving oxalates of Group I (100% trichobezoars), and none was found in the three subgroups of Group II, it may be assumed that the oxalates played no role in trichobezoar formation.

The consistent appearance of trichobezoars in rats on a synthetic diet without cellulose, compared with its absence in those animals on a synthetic diet with cellulose, seems to point fairly conclusively to the advantage of this type of inert material in the diet.

References

1. Armstrong, C. *Publ. Hlth Rep.*, 1939, **54**, 1719–1721.
2. Croxton, F. E., and Cowden D. J. *Applied general statistics.* New York: Prentice-Hall, 1945. Pp. 322, 324.
3. Eaton, M. D., Meikeljohn, G., and Van Herick, W. *J. exp. Med.*, 1944, **79**, 649–669.
4. Howell, S. R., Schlack, C. A., Taylor, B. L., and Berzinskas, V. J. Project X–418, Rep. No. 7, Naval Medical Research Institute, November 6, 1947.
5. Jungblut, C. W. *Proc. Soc. exp. Biol. Med.*, 1943, **43**, 479–486.
6. Meyer, B. J., and Meyer, R. K. *J. Mammal.*, 1944, **25**, 107–129.
7. Schweigert, B. S., Potts, E., Shaw, J. H., Zepplin, M., and Phillips, P. H. *J. Nutrition*, 1946, **32**, 405–412.
8. Shaw, J. H., Schweigert, B. S., McIntire, J. M., Elvehjem, C. A., and Phillips, P. H. *J. Nutrition*, 1945, **28**, 333–345.
9. Steinbach, M. M., and Duncan, C. J. *Proc. Soc. exp. Biol. Med.*, 1944, **44**, 288–290.

An Experimental Syndrome of Fatty Liver, Uric Acid Kidney Stones, and Acute Pancreatic Necrosis Produced in Dogs by Exclusive Feeding of Bacon

J. Groen

2nd Medical Service, Wilhelmina Gasthuis, Amsterdam

In the experiments to be described,[1] 9 dogs were fed on fat bacon exclusively. Two of these died after 2½ and 3 months, respectively. On postmortem examination they showed a severe fatty degeneration of the liver without significant changes in other organs.

Five dogs lived for periods varying between 5 and 7 months after the bacon diet was begun. At first these animals did well, but soon their appetite declined; they vomited occasionally and had to be fed forcefully. Occasionally they suffered from diarrhea. There was severe weight loss, and a peculiar kind of skin sores developed on the front and hind legs. Although the general condition became very poor and remained so for weeks, death occurred suddenly and often unexpectedly.

The postmortem examination of these animals revealed characteristic findings. The liver showed extensive fatty infiltration. In most cases only a few normal liver cells remained. These were located at the periphery of the lobules. Four of the 5 dogs had stones in the pelvis of the kidneys, in the ureters, or in the bladder which varied in size from a pinhead to a cornseed. They were thin and flat, sometimes round or polygonal in shape, and were of a greenish-yellow or brownish color. The bladder showed an apposition of stony material on the mucosa. The stones burned completely on heating and dissolved in alkali. Dried and powdered, the material gave a strong murexide reaction. Eighty-five per cent of the dry weight of the stones could be accounted for as uric acid. When the stones were dissolved in dilute ammonia, the solution filtered, and hydrochloric acid added, typical crystals of uric acid appeared.

In addition to these findings, 4 of the 5 dogs showed macroscopic and microscopic severe changes in the pancreas. The first animal showed extensive necrosis of the

[1] These experiments were carried out in the period 1938–40. With the German invasion of the Netherlands and the ensuing shortage of food, they had to be discontinued, and publication of the results was consequently delayed.

parenchyma cells; the next two had necrosis plus edema of the gland, with infiltration of polynuclear leucocytes and hemorrhages inside the septa; the fourth dog showed only pancreatic hemorrhages, without much necrosis or infiltration. Accompanying this acute pancreatic disease, all 4 dogs had fat necrosis of the adipose tissue around the pancreas and in the mesentery and omentum. These fat necroses had the typical aspect of white specks which is so characteristic of the fat necrosis that accompanies acute pancreatitis in the human. Three of the 5 dogs showed recent hemorrhages in the mucosa of the stomach or small intestine.

One other dog was fed 10,000 units of vitamin A and 5 mg of vitamin B_1/day in addition to the bacon diet. These vitamin supplements were unable to modify the course or the ultimate outcome of the experiment. This dog, which died after 7 months, had a fatty liver and acute necrosis with hemorrhages in the pancreas, fat necrosis in the omentum, and uric acid kidney stones, just as did the animals that had not received any supplement.

The last dog received 25 gm of raw liver daily for 13 months. At the end of this time it was still in perfect condition. The liver supplement was then replaced by 25 gm of raw pancreas daily. After 5 months on this supplement the animal died in a cachectic condition. Postmortem examination showed fatty degeneration of the liver. The pancreas showed hemorrhages and areas of inflammation. There were fat necroses in the omentum, and both kidneys contained uric acid stones. It appeared, therefore, as if 25 gm of raw liver had protected the animal, whereas 25 gm of raw pancreas had been unable to do so.

The severe fatty infiltration of the liver was obviously due to the combination of a high fat content of the diet and a lack of lipotropic factors. The finding of kidney stones consisting of uric acid is remarkable. The normal end-product of purine metabolism in dogs is not uric acid but allantoin, and only small amounts of uric acid normally appear in the dogs' blood and urine. Mann and his associates (*1*) have shown that the transformation of uric acid into allantoin in the dog takes place in the liver. In the liverless dog uric acid accumulates in the blood and is excreted into the urine. The same was found when the liver was damaged by chloroform or phosphorus intoxication. It seems likely, therefore, that the severe fatty infiltration of the liver had impaired its function in our animals and had acted as chemical hepatectomy. Moreover, many of the dogs had a low urinary output with a high concentration of solids and a very high urinary acidity. All these factors may have contributed to the precipitation of uric acid and the formation of stones in the urinary tract.

The hemorrhagic pancreatic necrosis in these animals had apparently occurred as a terminal event. Its explanation is uncertain. From the microscopical aspect one got the impression that the inflammation and hemorrhage had spread along the septa. In some of the sections the lumen of the pancreatic ducts appeared blocked by a material that could not be identified. It seems possible that obstruction of the ducts by this material has been the primary event after which necrosis, hemorrhage, and inflammation of the gland followed. Whatever the pathogenesis of the acute pancreatic necrosis may have been, it is interesting to note the association of acute pancreatic disease with fatty degeneration of the liver in these dogs. It is well known from human pathology that acute pancreatic necrosis occurs as a complication in patients with disease of the gall bladder and bile ducts, in alcoholics, and sometimes in diabetic coma. Fatty degeneration of the liver is a common feature in all these conditions. These experiments suggest that the presence of a fatty liver may play a part in the pathogenesis of acute pancreatic necrosis.

In a further communication the effect of the diet on blood and urine chemistry and blood morphology will be presented.

Reference

1. WILLIAMSON, C. S., and MANN, F. C. *Amer. J. Physiol.*, 1923, **65**, 267; MANN, F. C., and MAGATH, T. B. *Ergebn. Physiol.*, 1924, **23**, 212.

Photochemical Oxidation of Nicotine in the Presence of Methylene Blue

LEOPOLD WEIL

Eastern Regional Research Laboratory,[1]
Philadelphia, Pennsylvania

The photochemical oxidation of nicotine in the presence of methylene blue produces a compound which has not been completely characterized. During the course of this investigation, it was learned that a similar, if not identical, product had been isolated by W. G. Frankenburg (*1*) from the alkaloids of fermented tobacco. It was therefore deemed advisable to disclose our findings simultaneously.

If an aqueous solution of *l*-nicotine is irradiated in the presence of oxygen and a small amount of methylene blue, a rapid oxidation of the nicotine takes place which, in the dark, comes to a standstill. The effective wave length (around 6,700 A) coincides with the maximum absorption of the dye, and thus the "light-excited" dye can serve as a hydrogen acceptor, as shown by its rapid bleaching. The leuco methylene blue formed is reoxidized and serves continuously as a hydrogen acceptor. The oxygen required for the reoxidation of the reduced dye or, in terms of total effect, for the oxidation of nicotine thus serves as a means to follow the rate of the reaction.

An adaptation of the manometric technique of Warburg and Negelein (*3*) was used. White light of high intensity was passed horizontally through the glass wall of the water bath and reflected on the bottom of the vessel by a mirror placed at 45° under the respirometers. In general, 20 mg of the compound to be studied was dissolved in 1.5 cc of water and placed in the main chamber,

[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

and 0.5 cc of water solution of methylene blue containing 0.1 mg was placed in the side arm. After the vessel was filled with oxygen and the dye dumped into the main chamber, the oxygen uptake was measured in the usual fashion at the desired water-bath temperature. A rapid oxygen uptake took place which stopped sharply after about 4 hrs at 40°, when an equimolar amount of oxygen had been taken up. The optimum pH for the oxygen uptake was about 9. There was no CO_2 evolution.

Irradiation experiments under anaerobic condition in Thunberg tubes, to prevent reoxidation of the leuco dye, showed that the bleaching time is practically not affected at temperatures of 30°, 40°, 50°, 60°, and 70°, thus indicating a true photochemical reaction in this phase. The reaction appeared to be reversible, although it proceeded slowly, as in the thionine-iron system (*2*, *4*, *5*). The anaerobic photo-oxidation of nicotine, however, is strongly accelerated by increasing temperature, which would indicate the participation of a dark reaction in addition to the previously observed light-sensitive reaction.

The N—CH_3 group of the pyrrolidine ring seems to be important in the reaction, since under similar conditions *d,l*-nornicotine[2] acts sluggishly. Pyridine, β-picoline, β-vinylpyridine, nicotinic acid, and nicotinamide are unreactive. N—CH_3-pyrrolidine, however, which is a part of the nicotine molecule, is photo-oxidized in the presence of the dye at the same rate and to the same extent as nicotine itself. These experiments indicate that the chemical changes due to the irradiation are confined to the N—CH_3-pyrrolidine ring.

The product (obtained by larger-scale experiments) is a yellow viscous oil, not volatile in steam, practically insoluble in ether, but soluble in chloroform, in polar solvents, and in water. It is optically active ($\alpha_D^{20} = -35.2°$), indicating that the asymmetric carbon atom is not involved in the reaction. During the irradiation, the pH of the reaction mixture dropped from 10.4 to 6.8, suggesting that the strongly basic pyrrolidine nitrogen is involved in the reaction by forming, for example, an amine oxide. The elementary analysis of the ether-insoluble irradiation product of nicotine was: Calculated for $C_{10}H_{14}N_2O_2$: C, 61.85%; H, 7.21%; N, 14.43%; Found: C, 62.69%; H, 7.21%; N, 14.08%. Upon reduction with Zn and acetic acid in alcoholic solution, it was to a large part reconverted into nicotine (85–100%). Qualitative tests for aldehyde, keto, peroxide, and alcoholic groups were negative. The compound is not identical with oxy-nicotine. Further work is in progress to identify the product, but in the meantime, the following over-all equations are proposed for the reaction:

$$\text{(I)}\quad C_{10}H_{14}N_2 + M\text{—}B^{*} \xrightarrow{\text{light}} C_{10}H_{12}N_2 + M\text{—}B(H_2)^{\dagger}$$

$$\text{(II)}\quad M\text{—}B(H_2) + O_2 \longrightarrow M\text{—}B + H_2O_2$$

$$\text{(III)}\quad C_{10}H_{12}N_2 + H_2O_2 \longrightarrow C_{10}H_{14}N_2O_2$$

* Methylene blue
† Leuco methylene blue

Reaction I would represent the light reactions; II and III, the dark ones. An attempt to demonstrate the intermediate formation of H_2O_2, as required by reaction II, was not successful. Preliminary work indicated that the failure might be due to the high reactivity of certain tertiary amines with nascent H_2O_2.

[2] Kindly supplied by P. G. Haines, of this laboratory.

References

1. Frankenburg, W. G. *Science*, 1948, **107**, 427.
2. Rabinowitch, E. *J. chem. Phys.*, 1940, **8**, 551.
3. Warburg, O., and Negelein, E. *Z. phys. Chem.*, 1923, **106**, 191.
4. Weber, K. *Z. phys. Chem.*, 1931, **15**, 18.
5. Weiss, J. *Nature, Lond.*, 1935, **136**, 794.

Transformation Products of Nicotine in Fermented Tobacco

Walter G. Frankenburg

Research Laboratory,
General Cigar Co., Inc., Lancaster, Pennsylvania

One of the chemical changes concurring with the fermentation of cigar leaf tobacco[1] is a considerable decrease of the nicotine contained in the leaf tissues. Table 1 shows the average nicotine contents (30 samples each)

TABLE 1

Decrease of Nicotine Contents of Pennsylvania Cigar Tobacco for Various Crops
(Averages are based on analyses of 30 samples for each crop.)

Crop Year	Avg. nicotine contents (% of dry weights)*		Avg. decrease of nicotine due to fermentation (%)	Decrease of nicotine for individual samples	
	Before fermentation (BF)	After fermentation (AF)		Minimum (%)	Maximum (%)
1936	3.08	1.51	51	6	94
1938	2.82	1.76	38	7	72
1939	2.26	0.98	57	18	89
1941	3.85	2.04	47	27	83

* All values based on dry weights before fermentation.

of four crops of Pennsylvania Seedleaf tobacco, before and after fermentation. For the individual samples, the nicotine decreases range from 6 to 94% of the amount present before fermentation. A definite parallelism exists between the degree to which each individual sample has been fermented and the extent of its nicotine decrease. To the author's knowledge, no systematic studies have been published concerning the fate of the disappearing nicotine, except that occasionally volatilization of the alkaloid has been assumed without experimental proof.

In this laboratory, analytical studies have been conducted for several years on the nitrogenous components and particularly on the alkaloids and related substances in the leaf tissues of Pennsylvania tobacco. Specifically, we investigated the changes of these compounds resulting from fermentation.

[1] The fermentation of Pennsylvania tobacco has been described briefly by the writer (*Arch. Biochem.*, 1947, **14**, 157–181).

The principle analytical methods used for the study of the alkaloids and related pyridine compounds were:

(1) Distillations under varying conditions of alkalinity.

(2) Distillations from alkaline solutions in presence of nascent hydrogen (Devarda alloy).

(3) Precipitations with silicotungstic acid. Of these precipitates, the following values were determined: (a) the weights after drying at 110° C, (b) the nitrogen contents (by Kjeldahl), and (c) the losses of weight on ignition.

(4) Determinations of pyridine-nitrogen by the color reaction with 2,4-dinitrochlorobenzene (DCB), based on a modification of the method of Karrer and Keller (*1*).

(5) Total nitrogen determinations of the various fractions (Kjeldahl).

(6) Analytical determinations of specific tobacco alkaloids, e.g. treatments of fractions with nitrous acid, followed by distillation with weak alkali [for detection of secondary nitrogen in the pyrrolidine- (pyrroline-, pyrrol-) ring], preparation of picrates, etc.

Preliminary studies repeatedly gave indications of the presence, in the tissues of fermented leaves, of substances which are chemically related to, but not identical with, the tobacco alkaloids. These substances, in common with the tobacco alkaloids, are pyridine derivatives and form precipitates with silicotungstic acid[2] and colored products with dinitrochlorobenzene. Contrary to the alkaloids, they are not distillable from alkaline solutions, at least not without partial decomposition, and are not extractable from alkalinized leaf tissues or from alkalinized aqueous leaf extracts by the usual alkaloid solvents, such as ethyl ether, or petrol ether.

Finally, a fractionated extraction method was developed, leading to a fairly satisfactory separation of the various pyridine compounds in tobacco leaves. This method involves the following steps: Tobacco powder is alkalinized by wetting with NaOH-solution or by mixing with wet magnesium oxide. Fraction A is obtained by extraction with petrol ether; Fraction B, by extracting the residue of A with chloroform; and Fraction C, by extracting the residue of B with alcohol.

With respect to fractions A and B, it was concluded that:

(1) Pennsylvania Seedleaf tobacco contains, besides its main alkaloid nicotine, small quantities of other tobacco alkaloids (''secondary'' alkaloids). These are all contained in Fraction A.

The nicotine of Fraction A is separated from the remaining ''secondary'' alkaloids by treatment with nitrous acid followed by a weak alkali distillation. Preliminary studies indicate that the ''secondary'' alkaloids in Pennsylvana tobacco consist almost exclusively of compounds containing a secondary N-atom in their 5-membered rings, probably of nornicotine with possibly smaller amounts of myosmine.

(2) The leaf tissues of the *fermented* samples contain, as mentioned above, considerably less alkaloids, but appreciable amounts of the nonalkaloid-pyridine compounds. A part of these compounds is insoluble in petrol ether but soluble in chloroform. Accordingly, it is obtained in Fraction B. *The pyridine compounds in this fraction are closely related to, or identical with, the oxidation product of nicotine, containing two oxygen atoms, which has been obtained by Weil (2) via photo-oxidation of nicotine in the presence of methylene blue.*

The common properties of the compound (or compounds) obtained by Weil (I) and of the substances (II) extracted with chloroform (Fraction B) from fermented tobacco which was previously extracted with petrol ether are as follows:

(a) In precipitation with silicotungstic acid, the precipitates of (I) and (II) have the same spongy, grayish-white appearance and show after drying at 110° C the same nitrogen content as well as the same percentage loss of weight on ignition.

(b) On reduction with granulated zinc in 10% acetic acid, or with Devarda alloy in 5% NaOH, a considerable part (50–70%) is converted into nicotine which can be isolated by ether extraction or by distillation.

(c) (I) and (II), if reacted with dinitrochlorobenzene, form a reaction product which develops a purple color on addition of small amounts of KOH. The absorption spectrum of these colored solutions differs from that of the DCB-reaction products obtained with the known tobacco alkaloids. It is practically identical for (I) and (II). The bleaching of the colored solutions obtained from (I) and (II) on standing is considerably slower than that of the colored solutions obtained from the tobacco alkaloids and from nicotinic acid.

(3) *An appreciable part of the initial nicotine of the unfermented leaves is converted during the fermentation into the nonalkaloid compounds to be found in Fraction B.*

The amount of substance II in the fermented leaves is considerably larger than the amount present in the same sample before its fermentation. The increase corresponds, per sample, to 30–40% of the nicotine which disappeared during the fermentation.

Of the pyridine compounds present in Fraction C, a small part consists of nicotinic acid; the remainder, of a compound or compounds which, according to their color reaction with DCB, seem to be related to nicotinic acid. Further work is required to investigate the latter substances. Similar to compounds of Fraction B, the amounts of the C-compounds increase as a result of fermentation. This increase is estimated to correspond to 20–30% of the nicotine loss during the fermentation.

Accordingly, 50–70% of the disappearing nicotine can be found in fermented tobacco leaves as pyridine compounds of a nonalkaloid nature. Their production is obviously due to catalytic or enzymic factors which start to operate if the leaves are subjected to the fermentation process.

[2] This does not apply for nicotinic acid, which was also found as a minor component among the alkaloid transformation products.

References

1. KARRER, P., and KELLER, H. *Helv. Chim. Acta*, 1938, **21**, 463; see also VILTER, S. P., SPIES, T. D., and MATHEWS, A. P. *J. biol. Chem.*, 1938, **125**, 85.
2. WEIL, L. *Science*, 1948, **107**, 426.

IN THE LABORATORY

Intravenous Methylene Blue for Studying Fiber Degeneration in the Central Nervous System

WILLIAM H. FEINDEL and ANTHONY C. ALLISON

Department of Human Anatomy, University of Oxford

A technique based upon intravenous perfusion of methylene blue into an anaesthetized animal (*1*, *2*) permits a much wider application of the unique property of this dye in selectively staining nervous tissue *intra vitam*, and thus makes possible studies of both the general pattern and the cytological details of neural structure throughout the nervous system. It has been noted (*2*) that the value of this method is enhanced by its demonstration of degenerating fibers, both myelinated and nonmyelinated, in the peripheral nervous system, a feature of intravital methylene blue previously described in detail by Weddell and Glees (*3*), who used the technique of local injection of the dye.

The intravenous method has now been found to give a remarkably clear demonstration of degenerating fibers in

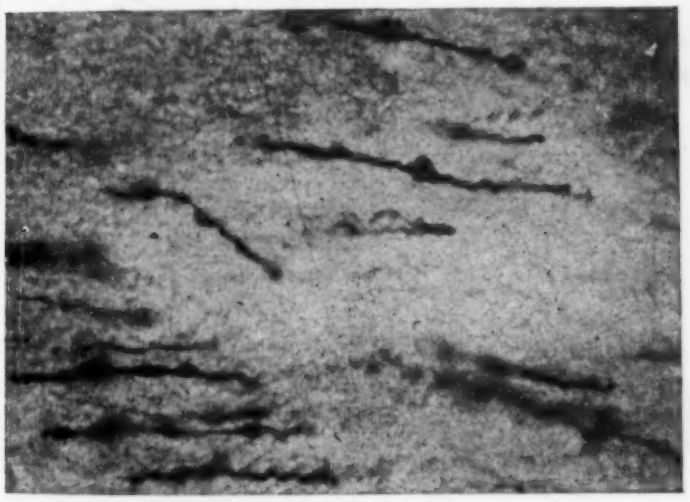

FIG. 1. Degenerating fibers in optic tract (×270).

the central nervous system. In rabbits perfused with methylene blue 5 days after section of one optic nerve, degenerating fibers in the optic pathways stand out distinctly as compared with normal fibers by reason of their more intense and metachromic staining. The contrast, even in macroscopic appearance, between the normal and degenerating optic nerves, is striking. In paraffin sections the degenerating fibers are rendered conspicuous both by their intense and characteristic reddish-purple shade of staining and by the morphological changes indicative of early degeneration, such as fibrillation and vesiculation of the axis cylinder, which they clearly exhibit (Fig. 1).

It is evident from these results that the method has a particular application to the problem of mapping out the fiber degeneration resulting from localized lesions in the central nervous system, and that it is therefore a technique likely to prove of great value in the field of experimental neurology.

The technical details of the method (*2*) have been modified to provide for more eritical handling of experimental material from the central nervous system. The use of a more concentrated solution of dye has obviated the necessity of injecting a large volume of fluid which may result in cerebral edema. In addition, more satisfactory fixation has been obtained by taking the tissues through formol-saline after the ammonium molybdate stage. Neither of these modifications interferes with successful staining. Further studies are now being made on a series of rabbits in which section of an optic nerve has been selected as a control lesion, and details of these studies will be published elsewhere.

References

1. FEINDEL, W. H., SINCLAIR, D. C., and WEDDELL, G. *Nature, Lond.*, 1948, **161**, 318.
2. FEINDEL, W. H., SINCLAIR, D. C., and WEDDELL, G. *Brain*, 1947, **70**, 495.
3. WEDDELL, G., and GLEES, P. *J. Anat.*, 1941, **76**, 65.

A New Series of Reagents for the Colorimetric Determination of Steroids[1]

LELAND C. CLARK, JR., and HASKELL THOMPSON

Samuel S. Fels Institute for Research in Human Development, Antioch College, Yellow Springs, Ohio

In an investigation of the factors involved in the antimony trichloride reaction for certain ketosteroids described by Pincus (*1*), a new series of colorimetric reactions involving the use of antimony trichloride, bismuth trichloride, and aluminum chloride has been discovered. Using the Friedel-Crafts ketone synthesis as an analogy for combining catalysts and acyl chlorides, as well as other reactants, a remarkably specific and waried series of reagents has been prepared. Although only a few of the reagents have been developed far enough to give quantitative color responses following the Beer-Lambert law, it seems desirable to report the results obtained thus far.

[1] The steroids used in this study were generously provided by Ciba Pharmaceutical Products, Inc., through the courtesy of E. Oppenheimer.

Since we had observed qualitative differences in the colors developed by steroid extracts obtained from different individuals, we were especially eager to standardize the procedure in order to evaluate these individual differences. Furthermore, it was felt that a series of reagents which were more or less specific for certain steroids would give additional valuable information. These views led to the discovery of the reagents and conditions reported here. Conditions were maintained for study of only those reactions which were, theoretically at least, capable of practical application.

In general, the reagents are prepared by combining the anhydrous metallic chloride and the "solvent" in such a way as to give a maximum concentration of the metal chloride. The ratio between the metal and the solvent in a given reagent mixture is a critical factor in determining the course of the color reaction.

The conditions for the initial reaction of the reagent with the steroid vary from 20 min at 0° C for $BiCl_3$-acetyl chloride to 60 min at 100° C for $SbCl_3$-phenol. The speed of the reaction for a given reagent can generally be judged by the colors developed in the reaction mixture, although occasionally a given steroid may show little or no evidence of reaction until the mixture is diluted. About 0.2 ml of reagent is allowed to react with 100 μg (0.10 mg) of steroid. Following the initial reaction the tube is cooled to room temperature, if necessary, and diluted with 10 ml of an appropriate solvent. The colors developed depend upon the dilution solvent as well as the reagent used. It has been found that the most generally useful diluent is a mixture of 10% acetic anhydride (less in some cases) in anhydrous benzene; this produces colors which are remarkably stable, some lasting without appreciable change for several days.

The absorption spectra obtained for androsterone and dehydroisoandrosterone under the conditions described by Pincus[2] are shown in Fig. 1. The peak at 550 mμ, which is high immediately after dilution with 95% acetic acid, gradually drops as the color changes from reddish blue to blue over a period of 60–90 min. The colors shown in Fig. 1 were obtained 90 min after dilution. The peak at 550 mμ was not found by Pincus, probably because of the wide band width (30 mμ) of the spectrophotometer he used. The spectra shown here were obtained with the Beckman spectrophotometer, using a 1-cm Corex cell and a slit width of 0.04 mm. Factors which apparently influence the absorption at 550 mμ and 610 mμ are the amounts of water and acetic anhydride in the $SbCl_3$ solution. For example, if $SbCl_3$ dissolved in 95% acetic acid is used as the reagent, the absorption obtained with androsterone at 550 mμ drops rapidly, while the peak at 610 mμ reaches the same value as that shown in Fig. 1. If the $SbCl_3$ is dissolved in acetic anhydride, *no color is produced by androsterone.* This color-inhibiting effect of acetic anhydride solutions of $SbCl_3$ is further illustrated by the finding that androsterone gives only a light blue color when *anhydrous* (redistilled) $SbCl_3$ dissolved in the acetic anhydride-acetic acid solvent recommended by Pincus is used as the reagent. It would therefore appear that a more reproducible reagent can be prepared by

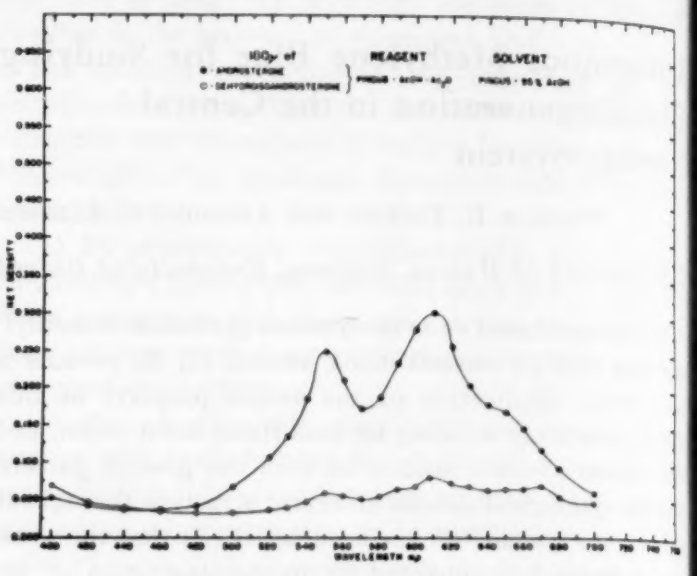

FIG. 1

using components of known water content rather than relying upon a certain amount of acetic anhydride to destroy variable amounts of water in the $SbCl_3$ being used.

These and other factors explain why some batches of $SbCl_3$ reagents fail to give colors following the Beer-Lambert law. To obtain further information concerning the relative importance of the different variables,

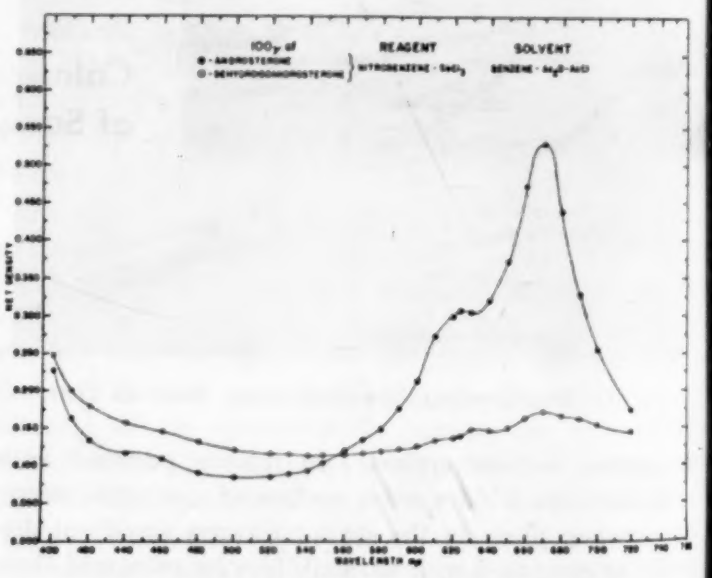

FIG. 2

many other conditions have been tested, and some of these results are summarized below.

Since nitrobenzene is an excellent solvent for $SbCl_3$ and, in fact, probably forms an oxonium complex with it, a reagent containing 26 gm of $SbCl_3$ in 5 ml of nitrobenzene was heated with steroid samples for 40 min at

[2] Thirty-eight gm of $SbCl_3$ was dissolved in 10 ml of a mixture of 9 parts of glacial acetic acid and 1 part of acetic anhydride. The antimony trichloride was used, as received from a freshly opened glass-stoppered jar (Coleman and Bell Company, Norwood, Ohio).

100° C. Upon dilution with benzene, containing 0.025% acetyl chloride and 0.025% acetic anhydride, an intense blue color is obtained with androsterone, while a light green color is given by dehydroisoandrosterone. The absorption spectra, shown in Fig. 2, illustrates the fact

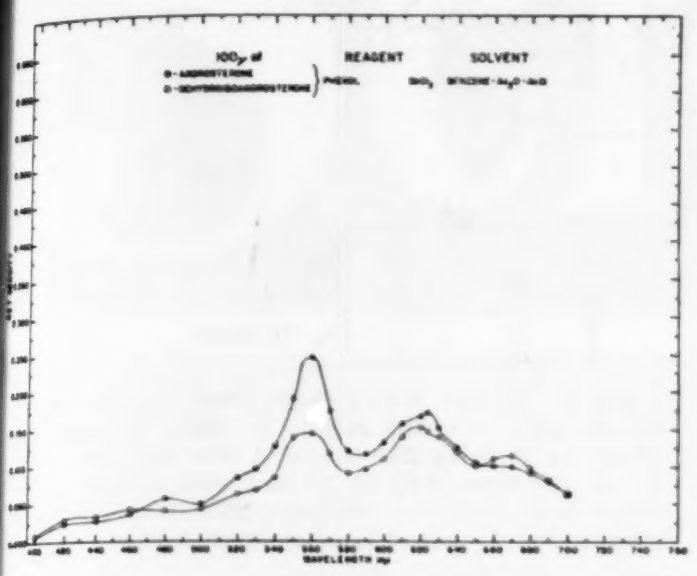

FIG. 3

that the color is extremely intense and that the peak has been shifted to 670 mμ. The colors obtained were stable for several days.

The use of a solution of $SbCl_3$ (52.1 gm) in phenol (10.2 gm) produces colors which have nearly equal intensity for androsterone and dehydroisoandrosterone (Fig. 3). The reddish blue colors produced upon dilution gradually become more blue and, again, are stable for

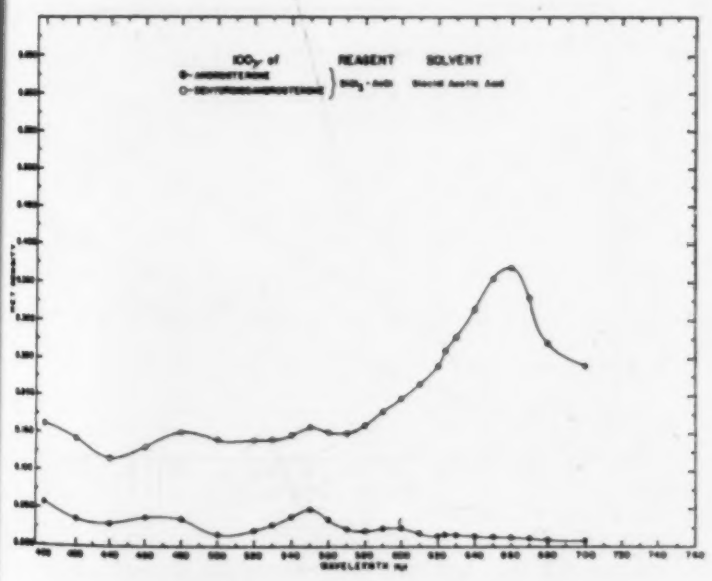

FIG. 4

long periods. If the acetyl chloride is not added to the benzene-acetic anhydride diluent, the colors are blue immediately upon dilution and dehydroisoandrosterone gives about 80% of the color of androsterone at the 624-mμ peak. Similar results are obtained using 95% acetic acid as diluent, but the colors fade more rapidly.

When $SbCl_3$ is dissolved in acetic anhydride, no color is produced with androsterone, as mentioned above, but an *intense blue color is obtained with dehydroisoandrosterone*. A similar effect is obtained using a solution of $BiCl_3$ in acetyl chloride, the spectra for which are shown in Fig. 4. This reaction shows a high degree of specificity and may prove valuable in measuring this steroid in certain pathological conditions.

A solution of $SbCl_3$ in succinic anhydride, using a 10% solution of acetic anhydride in benzene as the diluent, produces a deep blue bolor with androsterone, a very light blue color with dehydroisoandrosterone, a *blue color with a strong red fluorescence with testosterone*, a *pink color with a green fluorescence* (*like eosin*) *with* α-*estradiol*, and no color with Δ^4-androstenedione. Similar results are obtained using phthalic anhydride as the solvent for the $SbCl_3$.

A single reagent prepared by heating 10 gm of anhydrous aluminum trichloride with 10 ml of benzoyl chloride and dissolving the product in 40 ml of nitrobenzene illustrates a further extension of these reactions. In this case, the only steroid out of 15 tested which gave a color was Δ^4-androstenedione-3, 17, which produced an intense red solution (maximum at 570 mμ) when diluted with glacial acetic acid.

It seems plausible to expect that some of the other Friedel-Craft catalysts, such as $SbCl_5$, $SnCl_4$, $TiCl_4$, $TeCl_2$, $TeCl_4$, $ZnCl_2$, and $CbCl_5$, will give new color reactions having other degrees of specificity and intensity when combined with various solvents such as the acyl halides and anhydrides, organic acids, nitrobenzene, and phenols. As yet, the mechanism of the reaction is not understood. However, the fact that some of the colored products can be adsorbed on aluminum oxide, while others, particularly those obtained with $BiCl_3$ tend to precipitate on standing for 24 hrs, may facilitate isolation and identification of the colored end-products. The insolubility of the colored substance obtained with bismuth indicates that the colored product may be a metal complex with the steroid, since bismuth compounds are generally less soluble than antimony compounds.

Preliminary results indicate that at least some of the reagents mentioned can be applied to the measurement of steroid mixtures such as are obtained in the ketosteroid extracts of urine. It has been found that the colors can be destroyed by adding a small amount of moist U.S.P. ether to the colored solution, thus making possible the determination of the "blank" colors of the extract itself. If turbidity develops, the solution may be cleared by adding a drop of concentrated hydrochloric acid.

Further work, now in progress in this laboratory, includes testing the qualitative properties of various other reagents, refining those of promise, and applying the methods to the determination of steroids in urine extracts. The results will be published in detail at a later date.

Reference

1. PINCUS, G. *Endocrinology*, 1943, **32**, 176–184.

A Radio Frequency Coupled Tissue Stimulator

OTTO H. SCHMITT

Departments of Physics and *Zoology*,
University of Minnesota

Electronic technique has advanced to the point where it is relatively easy to provide an electrical stimulus of almost any desired wave form, amplitude, and timing. There has been no satisfactory answer, however, to the problem of isolating these stimuli both conductively and capacitively from ground. Such isolation, if achieved, at once eliminates several of the persistent difficulties familiar to all electrophysiologists. Amplifiers may once again be operated grounded or, if used differentially, permit new freedom from shock artifact; any number of stimuli of assorted form and timing may be applied simultaneously or in sequence; and different impulses may be applied at various points on the tissue without any nonphysiological interaction.

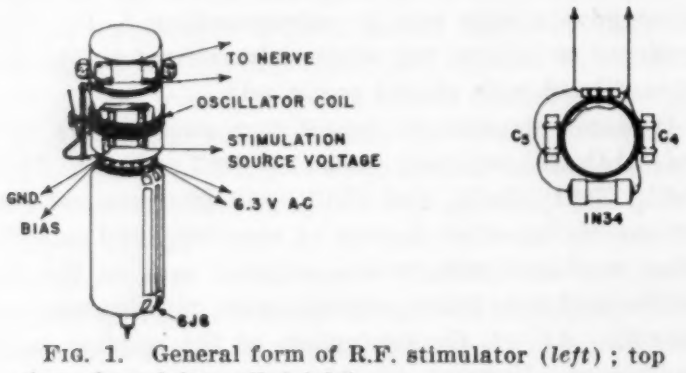

FIG. 1. General form of R.F. stimulator (*left*) ; top view of receiving coil (*right*).

The desired isolation may be provided surprisingly simply through utilization of a high-frequency radio link, the desired stimulation wave forms being converted to amplitude or frequency modulation of a carrier frequency and this carrier energy being reconverted, after transmission across an isolating air gap, into the desired stimulus by a tiny demodulator utilizing a germanium varistor as a linear rectifier.

In the primitive form in which the apparatus is now being used in our studies on single nerve fibers, the apparatus takes the form sketched in Fig. 1. It consists of a single miniature or subminiature tube with an associated grounded-plate Hartley oscillator circuit tuned to about 5 MC and a receiving coil tuned to the same frequency and with attached demodulator and R.F. filter.

The circuit is that shown in Fig. 2. It will be noted that no power supply except 6 v for the filament is required, since all power for the oscillator is drawn from the stimulator itself. The usual thyratron, or hard tube stimulator, is amply capable of supplying the necessary energy because the voltage delivered to the tissue circuit under typical conditions is nearly one-third as great as the incoming voltage. The R.F. stimulator is thus nearly as efficient as usual coupling transformers and may be used interchangeably with them if an additional prong for filament voltage is included in the cable connection. Some care must be taken to shield against direct transfer of R.F. voltage to the tissue circuit.

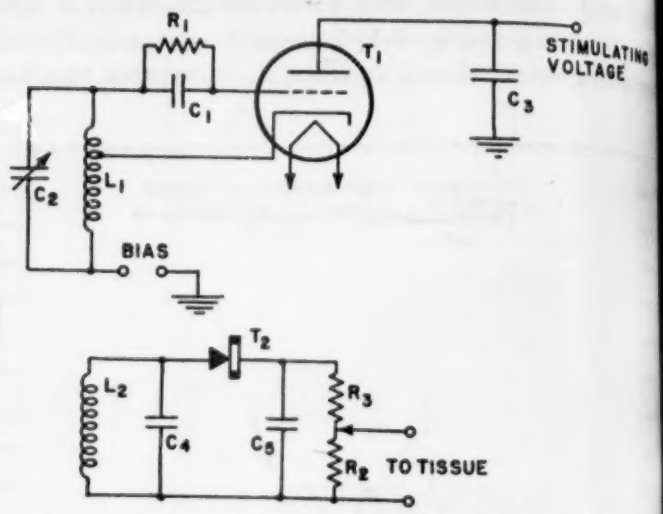

FIG. 2. C_1, 100 MMF; C_2, 25 MMF; C_3, 30 MMF; C_4, 20 MMF; C_5, 100 MMF; R_1 22K; T_1, 6J6; T_2, 1N34; L_1, 36 turns #32 enameled wire bank wound on ¾" i.d. coil form, winding ¾" long with cathode tap 6 turns from grid; L_2, 30 turns #32 enameled wire, circular coil ¾" i.d. of circular cross section.

The over-all linearity of performance is demonstrated in Fig. 3, which plots stimulator output voltage against input voltage. Precise linearity for weak stimuli is not obtained unless a small DC bias is applied to the input to bring the tube up to nearly oscillating voltage. It is customary to adjust the voltage-dividing resistors, R_2 and R_3, to bring the stimulator into its linear range for the general stimulus strength being used. Stability of the stimulator is within a fraction of a per cent after a short warm-up period, and adjustment is almost entirely noncritical. For very short pulse stimulation (less than 0.1 m sec pulses) special care must be exercised in the design of the plate by-pass circuit, and it is advisable to increase the oscillator frequency.

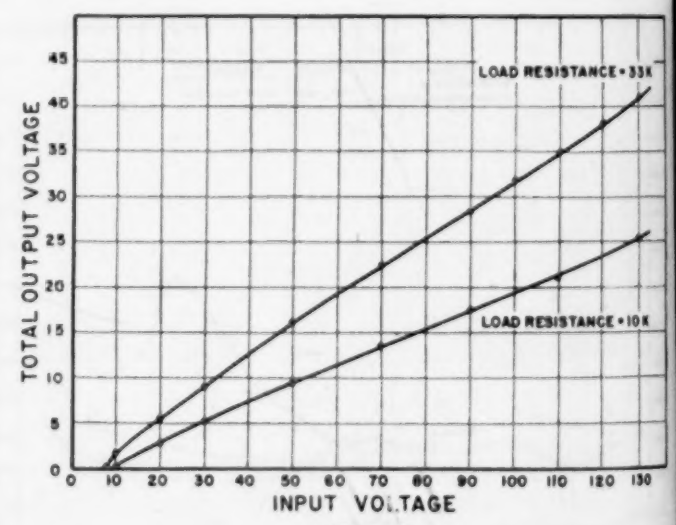

FIG. 3

While this preliminary note will not discuss them, many modifications of the stimulator for special purposes are possible. In nearly all cases the design can be made almost completely on paper, as the stimulator works in a region where electrical behavior is easily predictable. A more detailed paper presenting some of the design analyses will be published in the near future.